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THE HISTOPATHOLOGY OF THE UTERUS IN RELATION TO THE SOCALLED ESSENTIAL OR IDIOPATHIC UTERINE BLEEDING

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THE essential uterine bleeding is defined as that in which there is an absence of any detectable clinical pathology in the entire female genital tract, save for possible enlargement of the uterus. This affliction has been called "chronic metritis," "fibrosis uteri," "myopathia hæmorrhagica," "pseudo-metrite" (French), "sclerose uterine" (French), etc., according to the views of various authors upon the cause or chief pathological feature observed by them.

Numerous papers and monographs have been written upon the subject, a great amount of research has been done in this direction, and yet at the present time we cannot say that the precise cause of this condition is known, and as it often happens, when the etiology is obscure, numerous theories are offered in its explanation by various authors only to be disproved and cast aside by subsequent investigators. Nevertheless, the multitude of work has accomplished a great deal. It has taught us the minute histology of the female genital tract at the various phases of the woman's sexual life; it has clarified the nomenclature and has suggested a clinical course which has yielded satisfactory results in selected cases. This study was undertaken in order to learn what is or what is not the cause of the bleeding and we think that we have succeeded in the latter. The material is comprised of 25 specimens removed surgically for various reasons, such as bleeding, prolapse of the uterus, mistaken diagnoses of uterine fibroids, etc. In 16 cases there was vaginal bleeding of varying severity and duration, lasting from several days to 2 years at both extremes, being of menorrhagic and metrorrhagic type and sometimes uninterrupted for several weeks to 2 months. In one of the cases a preliminary curettement was performed for diagnostic purposes shortly prior to the hysterectomy, with no amelioration of symptoms. In another case the uterine cavity was cleaned and radium inserted without a noticeable effect upon the hæmorrhage. In 9 cases there was no bleeding at all. In one of them, the menstrual periods occurred every 2 weeks and were of moderate duration and amount. In another there was amenorrhœa of 3 to 4 months, followed by a normal menstrual flow. These 9 non-bleeding uteri served as controls, for we aimed to compare the histopathology of the bleeding uteri with that of the non-bleeding, although we did not consider the last group normal, because some of them were prolapsed, others considerably enlarged, and the only clinical distinction between those two groups was the presence or the absence of bleeding.

Of interest also were the findings of associated pathology in the rest of the genital tract, such as in the ovaries or tubes, or both these structures, and whenever it was possible, we gave the data about the condition of the

appendages. In the bleeding group, we found pathological changes in the ovaries, or in the tubes, or in both of these organs. In only 4 cases was there no associated pathology in the entire genital tract, while in 2 cases there was chronic salpingitis only. In 10 cases there were pathological findings in the ovaries, 4 times the ovaries alone deviated from normalcy, 4 cases showed abnormalities in the ovaries with accompanying chronic salpingitis, in 2 cases in addition to the changes in the ovaries, small intramural fibroids were found. These fibroids were so small and insignificant that they escaped not only clinical detection but they were invisible during the operation, their presence being discovered only upon cut section of the specimens. Because in all of these cases, in which chronic salpingitis and small intramural fibroids were found during the operation or in the laboratory, the bleeding was considered idiopathic from the clinical standpoint, we included them in our study.

To summarize the condition of the adnexa in this group, we may say that of 16 cases 10 or 60 per cent showed pathological changes in the ovaries, while in 36 per cent of the total the tubes were involved with or without ovarian pathology. The ovarian pathology was described as cystic ovaries and serous cysts (we did not observe ourselves the pathological condition of the ovaries as for obvious reasons many of them were left *in situ* by the surgeons).

The majority of the patients in the bleeding group were in the fourth decade: 10 patients in the fourth decade, 4 in the fifth, 1 in the sixth, and 1 in the seventh decade; in the total of 16 patients parity varied as follows: nulliparæ, 5; ii-paræ, 3; iii-para, 1; vi-para, 1; vii-para, 1; ix-para, 1; xv-para, 1; unknown parity, 3. Of the 16 cases, there were 5 nulliparous, 8 multiparous patients, and the parity of 3 was not learned from the history available to us. The shortest period of bleeding was 4 days, the longest 2 months, the majority bled 3 to 4 weeks continuously.

Grossly, the specimens were found to be enlarged, firm, and of normal shape. On cut section, fibrous bands could be seen by the naked eye, the blood vessels were enlarged in caliber and protruded above the surface of the mesometrium. This picture was not the rule, however. In some cases the uteri were found small or of normal size with no blood vessels seen macroscopically. The size of the uterine cavity varied from 5 to 10 centimeters. The endometrium was found thin or of normal thickness in all but 2 cases in which it was polypoid and thick. We endeavored to study minutely every histological structure of the entire uterus. In the endometrium we paid particular attention to the condition of the glands and stroma; in the mesometrium, the fibrous tissue, elastica, and blood vessels were scrutinized. In order to bring out to the best advantage the various structures, we stained each specimen with hemalum and eosin, according to the usual technique, with van Gieson in order to differentiate fibrous from muscle tissue, and with Weigert's stain for elastic tissue.

In the early days in the history of irregular uterine bleeding various authors had been observing changes in the uterine mucosa which they thought were either inflammatory or hyperplastic in nature. Such changes were observed by Recamier in 1850. Olshausen, in 1875, described them as "chronic hyperplastic endometritis" or "endometritis fungosa"; Bishoff (quoted from W. Shaw) as "adenoma diffusum." Ruge, in 1880, spoke of 3 forms of endometritis which he held responsible for irregular uterine bleeding, namely: 1, interstitial, 2, glandular and 3, mixed.

Ruge's views enjoyed wide popularity until Hitschmann and Adler, in 1907, proved conclusively that the condition of the mucosa which Ruge considered inflammatory and pathologically hyperplastic was physiological for certain phases of the menstrual cycle. These 2 authors put the knowledge of endometritis on a scientific basis, postulating that infiltration with leucocytes and especially with plasma cells is the prerequisite of an inflammation in the endometrium as elsewhere in the body. Novak, Novak and Martzloff found characteristic changes in the corporeal mucosa in cases of functional uterine bleeding. These changes, according to these authors, are so constant and typical as to form, if not a clinical, at least a pathological, entity.

W. Shaw observed in 25 per cent of his series alterations in the mucosa which corresponded

closely to those described by Schroeder in cases of "myopathia hæmorrhagica," a detailed description of which will be given below.

In the bleeding group of our series the most marked feature observed was the hyperplastic condition of the glands (the term "hyperplasia endometrii" we do not use in the special sense of the word to describe a pathological entity, but in the same sense as it is employed in general histopathology).

In 10 cases, the glands were seen uneven in size, lined with cylindrical epithelium, the nuclei of which were intensely stained with basic stains. In all these 10 cases the majority of glands were dilated and not infrequently lined with many layered cylindrical epithelium. In 5 cases, or in 35 per cent, some of the glands were dilated into cysts, which lost their glandular appearance. These cysts were most frequently lined with cuboidal epithelium and occasionally their epithelium was flattened out. The lumina of those cysts contained amorphous débris and large epithelial cells. Along with these dilated glands we have observed in some of the specimens tortuous glands with stems of connective tissue, lined with cylindrical epithelium, trespassing upon the lumina and giving them a papillary appearance. In 2 cases, premenstrual changes were seen in the same specimens in which there were also features of hyperplasia of the endometrium. Frequently we observed an increase in the number of glands. These lay very close to each other, with the stroma scant between them. The hyperplastic and hypertrophic changes varied greatly in these 10 specimens. Sometimes the only deviation from the normal state was the very tall, intensely stained epithelium of the glands, the mucosa being sound otherwise. Occasionally goblet cells intermingled with the ordinary cylindrical cells and more frequently vacuoles were seen. The stroma we have found loose in texture in some specimens, dense and cellular in others. Frequently, especially in those cases in which the glands were distinctly dilated, we noticed mitotic figures in the framework of the mucosa. A peculiarity seen in some of the specimens was large mononuclear cells with a wide protoplasm, the nuclei of which were displaced to one side. Necrotic areas we met three times in the bleeding group, most prominently in the case that received radium some time prior to the hysterectomy. In some specimens, the framework of connective tissue stroma was increased in amount and appeared thicker and coarser than usual. This fibrosis of the endometrium was particularly well exampled in 3 cases. In the bleeding group there were 4 specimens which revealed no demonstrable deviation from normal in the endometrium, except the presence of cystically dilated glands in 2 of them. None of these 4 cases had any ovarian alterations. In the 10 cases which showed some degree of glandular or stromal hyperplasia, 9 were associated with ovarian abnormalities and 1 had no ovarian pathology whatsoever. In 1 case only we observed mononuclear cells of large size, in which the nuclei were very pyknotic and surrounded by a light halo, which gave the impression of being plasma cells. This was the only specimen in the bleeding group which gave evidences of a chronic inflammatory process in the endometrium (this case received radium treatment 6 months prior to the laparotomy).

Besides authors who believed in endometrial changes as the main feature of idiopathic uterine bleeding, there were others who, quite early in the history of this question, sought the cause of bleeding in the mesometrium and focused their attention upon every constituent of this structure. The term itself "chronic metritis" as this condition has been and is still called, implied that the etiological factor was localized in the myometrium and was of inflammatory nature (at the present "chronic metritis" is not used in that sense).

Prior to 1902, many works upon "chronic metritis" contained a description of the uterine wall in which the amount of fibrous tissue was increased, but the early writers did not ascribe much importance to that fact. On the contrary, Theilhaber and Meier in 1902 considered the increased amount of fibrous tissue as an etiological factor in idiopathic uterine bleeding. They thought that the decreased power of uterine contractions or as they name it "insufficientia uteri" was responsible for the bleeding. They contended that the uterine contractions play an important rôle in the circulation of this organ, assisting the outflow

of the venous blood toward the heart, much as the muscles of the lower extremities do in the venous circulation. When there is an insufficiency of the uterine muscle, venous stasis occurs as its result, which in turn leads to overnutrition of the organ and to hypertrophy of the connective tissue. The authors also called attention to the fact that in old age the amount of fibrous tissue is increased physiologically. Lorenz, in 1903; Palmer Findley, in 1905; Hirsch, in 1909, fully supported the views of Theilhaber upon myofibrosis uteri as the cause of its insufficiency. Schiekele and Keller were among the first and strongest opponents of the fibrosis theory. They devised a method of quantitive determination of the amount of fibrous and muscle tissues. Using their method which, although not exact, is superior to the ones employed hitherto, the authors came to the conclusion that the amount of fibrous tissue has no relationship to the intensity of bleeding, that parous uteri contain more fibrous tissue than nulliparous and this amount increases with parity.

Viewing our material from the standpoint of deviations in the content of fibrous tissue, we observed decided increase in this structure in the majority of bleeding uteri. In all but 4 cases we thought the amount of fibrous tissue exceeded the muscle; in the aforementioned 4 cases the amount of fibrous tissue equalled that of the myomatous. The fibrous structures were particularly increased around the blood vessels, forming thick, coarse, bright red bands around the large arteries in a van Gieson's stain.

In some areas this increase was so pronounced as almost to obscure the muscle tissue. Next to the vascular layer, we saw the greatest amount of fibrous tissue in the subserous layer, where the fibrous bands formed a net, which encircled the muscle. Where the fibrosis was pronounced, we observed also fine delicate strands of fibrous tissue embracing small groups of muscle bundles or even individual cells. The most extreme increase of fibrous tissue was observed in the 3 following cases: (1) patient aged 55 years, xv-para; (2) patient aged 63 year , parity not known; (3) patient aged 32 years, iii-para. In many cases of considerable fibrosis, there was an appreciable amount of it in the media of the larger arteries. We experienced great difficulty in judging the amount of fibrous tissue in a given specimen, the reason for it lying in the fact that there is normally a large amount of fibrous tissue in every uterus. In an adult young woman, the amount of fibrous tissue of the uterus equals one-third of the mesometrium. In infants, children, and senile women, fibrous tissue forms two-thirds of the bulk of the mesometrium (Theilhaber). If we take this into consideration, we will realize the difficulty in detecting an additional amount, unless it be considerable or a quantitive method be used. In some of the cases in which we thought the amount of fibrous tissue exceeded the myomatous we easily could be convinced that the reverse was the truth. We are, therefore, taking our findings with some reservations.

Much less trouble was had in estimating the amount of elastic tissue. It has been noticed that in parous uteri the amount and distribution of elastic tissue is so altered as to permit a diagnosis of parity with certainty. In parous uteri the internal elastic lamina loses its smoothness and evenness, it is much thicker and there is a distinct increase of elastic tissue around the middle tunica. The fine fibrils of elastica of nulliparous uteri are transformed after parturition into thick, coarse strands which traverse the mesometrium in various directions. It is believed that during pregnancy all the constituents of the mesometrium undergo hypertrophy and during puerperium they undergo retrogression but not to the same degree—myomatous tissue involutes the most, fibrous the next, elastic tissue the least, hence pregnancy is associated with a permanent increase in elastic tissue (Szasz-Schwarz, Anspach). Some authors, among whom are Szasz-Schwarz, Anspach, Goodall, W. F. Shaw, and others, attempted to study cases of irregular uterine bleeding with special reference to the elastic tissue.

In our series in nulliparæ the elastic tissue was seen distinctly in the internal elastic lamina of the arteries and in very small amount in the mesometrium as fine delicate fibrils. In the parous uteri on the contrary, clusters and bunches of thick, coarse groups

of elastica were found in the mesometrium and in the media of the large arteries, also the internal and external elastic laminæ were greatly thickened. In a few of the multiparous specimens, the muscle of the media almost disappeared and was replaced by elastic tissue. The largest amount of it was seen in multiparous women of advanced ages, such as 63, 55, and 49 years, but on the other hand, a woman of 32 years, ii-para, with no history of abortions had an extreme quantity of elastica. As we shall see later the same character and distribution of elastic tissue was found in the non-bleeding group, and in no way, we thought, did this structure differ in either of the groups.

Considerable attention was paid to the condition of the blood vessels in cases of "chronic metritis" by the early students of this question. Cruveilier, Rokitansky (quoted from Wittek) considered the fragility of the blood vessels in elderly women as a cause of hæmorrhagic infarction of the uterine wall, which they called "apoplexia uteri." Cornil (quoted from Wittek), Pichevin and Petit and Marchesi described cases of uterine bleeding in which there were prominent sclerotic changes in the blood vessels. The most popular advocate of arteriosclerotic changes in the uterine blood vessels was Reinecke, whose views in 1897 achieved the importance of a theory. The author believed the changes observed by him in the blood vessels to be of arteriosclerotic character and moreover of etiological moment in the bleeding of elderly women. Both Cholmogoroff, in 1900, and Wittek, in 1906, supported Reinecke's theory. The findings and views of Reinecke were subjected to revision by subsequent authors who thought the blood vessel changes were of physiological nature for old age and multiparity (Theilhaber, Findley, Hirsch, Pankow, etc.).

In our own study we have found the blood vessels thickened from extreme to moderate in 11 cases. The most marked changes were observed in a xv-para, aged 55 years, in a multipara of 63 years, and in a ix-para, of 37 years. A moderate thickening we saw in a nulliparous woman who underwent eight abortions. The thickening involved the media and adventitia mostly, but on a few occasions we found the intima also thickened. The thickening of the latter structure is best demonstrated by the Weigert's stain for elastic tissue. Hyalinized areas of the media were observed in the same cases in which hyalinization of the myometrium was seen. The blood vessels were gaping in some cases, narrowed in others, and occasionally their lumina were completely obliterated (all these phenomena could be observed in the same specimen).

In 8 cases, or in 50 per cent, a distinct endometriosis was observed. Within the mesometrium at a short distance away from the mucosa and not connected with it in any manner, there were found one or more glands, surrounded by endometrial stroma.

In no case were there seen inflammatory lesions in the mesometrium.

Summarizing the histological findings in the bleeding uteri, we may say that:

1. Hypertrophic and hyperplastic changes in the endometrium of various degrees, were seen in 10 cases or in 70 per cent of the total, in which the mucous membrane was available for study. (In 2 cases the endometrium was not seen.) In 2 cases, besides signs of hyperplasia, early premenstrual changes were noticed.

2. Cystic glands were seen distinctly in 5 cases, or in 35 per cent. In others the cysts were hardly distinguishable from moderately dilated glands, or absent altogether.

3. Necrosis of the stroma was found in 3 cases or in 21 per cent and distinct signs of chronic inflammation of the mucosa were observed in 1 case only, in which radium had been inserted.

4. Fibrosis, excessive to moderate, was the rule. In 12 cases the amount of fibrous tissue exceeded that of the myomatous, in 4 cases they were equal. The extreme amount was observed in aged and multiparous women, with few exceptions.

5. The elastica was found increased in amount in parous uteri only, and this amount bears no relationship to the severity of bleeding. It seems that the amount of this structure depends not only upon age and parity, but is subjected to individual variations.

6. Blood vessels were found thickened in the majority of cases, namely in 11, but most prominently in aged and multiparous women.

7. Endometriosis (the infringement of the mucosa in the mesometrium at a short distance from the normal borderline) was encountered in 8 cases, or in 50 per cent.

We shall analyze here very briefly the non-bleeding group of cases and compare the findings with those of the bleeding variety. There were 9 cases in the non-bleeding group, their ages ranging from 19 to 55 years.

Decade	Patients
Second	1
Third	1
Fifth	4
Sixth	2
Unknown	1
Total	9

Parity	Patients
Nullipara	1
i-para	2
iii-para	1
iv-para	1
v-para	1
Unknown	3
Total	9

Of these 9 cases, operated upon for other than bleeding reasons, 2 had follicle cysts in the ovaries, 1 had a serous ovarian cyst. In the same cases, chronic salpingitis was diagnosed on the operating table by thickening of the tubes and afterward microscopically. In other words, in 33 per cent there were found ovarian pathological changes and signs of mild chronic salpingitis. In 2 of these 9 cases, the adnexa were not inspected, because the surgery was done by the vaginal route, which leaves 3 of 7, or 42 per cent, with ovarian and tubal pathology. In the non-bleeding group we found practically the same type of pathological changes as were observed in the bleeding cases, but not in the same degree.

We will not discuss in detail the histopathology of the bleeding group but, briefly summarizing the histological findings in this group, we may state that:

1. The endometrium was found hyperplastic and hypertrophic in 3 cases, or in 33 per cent, with signs of early premenstrual changes in 2 cases.

2. Cystic glands were seen in 5 cases or, in 55 per cent, the cysts were met with in hyperplastic and otherwise normal endometrium.

3. An increased amount of fibrous tissue of such degree as to exceed the muscle was detected in 4 cases, or in 44 per cent.

4. Elastic tissue was increased in amount in all parous uteri in a varying degree.

5. Thickening of the blood vessels was seen in 6 cases or in 66 per cent of the total.

6. Endometriosis was observed in 4 cases, or in about 44 per cent.

7. No necrosis or signs of inflammation in the endometrium were seen.

DEDUCTIONS

We would like to discuss here briefly the occurrence of unusual features observed in cases of both groups.

In our material, cystic glands were seen in a number of cases in the bleeding as well as in the non-bleeding group. It was observed more frequently in combination with signs of hypertrophy and hyperplasia of the endometrium, although we met large cysts in some cases in which the mucosa was atrophic, as in an elderly woman of 63 years. In some cases the stroma was dense and cellular, the glandular epithelium tall—cylindrical with conspicuous hyperchromatic nuclei; nevertheless there were no distinct cysts, but some of the glands were somewhat dilated while preserving their shape. In other words, dilatation of the glands is in our experience a more constant feature of hyperplasia than formation of cysts. In a few cases of the non-bleeding group the endometrial stroma and glands were considered normal; nevertheless, distinct cysts were seen.

We cannot, therefore, consider cystic glands as a constant and indispensable feature of hyperplastic endometrium, although a very frequent occurrence. Neither are these cystic glands a characteristic pathological finding of the endometrium in bleeding uteri. We are calling attention to the frequency with which we encountered hypertrophic and hyperplastic changes in the bleeding endometrium. It is true that sometimes these changes were not prominent, however, they were noticeable on careful examination. If there were bleeding cases with no signs of proliferation in the mucosa, there were as well 3 cases in the non-bleeding group which revealed distinct features of hyperplasia of the uterine glands. In 1 case only, belonging to the bleeding group, we saw plasma cells in the endometrial stroma. Because of the fact that the same patient underwent radium treatment 6 months prior to the operation, we are inclined to believe that the endometritis is a complication of the treatment rather than the etiological factor in bleeding. As to the fibrosis of the mesometrium, we may say that we found this feature

in both groups but in a higher degree and frequency in the bleeding group. The most extreme quantity was seen, as we have mentioned before, in aged multiparous women in both groups; but this was not a strict rule, for an excessive amount of fibrous tissue we observed in a woman of 32 years, iii-para. Two nulliparæ of comparative youth, ages 33 and 35 years, respectively (both of them from the bleeding group), had an amount of fibrous tissue which we thought exceeded that of the muscle. But these nulliparæ were gravid sometime in their past. We must, therefore, point out that in the bleeding group the increase in this structure was observed in younger women who never bore full term children. In the non-bleeding group the increased amount of fibrous tissue was not so conspicuous as in the former group. The largest amount of it we observed in women of advanced ages, but in one instance a pronounced fibrosis was seen in a 19 year old nullipara, whose tubes were inflamed. From our small material we cannot conclude that age and parity are the only factors influencing the amount of fibrous tissue. The facts that ablation of the function of the ovaries by surgery or radiation checks the bleeding in a large number of cases, that some cases of prominent fibrosis do not bleed, and also that the amount of fibrosis is not proportionate to the amount and severity of bleeding, make us believe that fibrosis, although frequently met with in bleeding uteri, is not the cause of hæmorrhage but the accompanied feature of it.

In regard to the amount and distribution of elastic tissue in both groups, no essential difference between the bleeding and non-bleeding cases was observed. The parity and age had more to do with the amount of this structure than the absence or presence of bleeding. In general it was observed that the greater the parity the more elastic tissue the uterus contained, but this rule permits a few exceptions. In some instances we saw uteri of smaller parity having a greater amount of elastic tissue, than the ones of greater parity. In 2 cases, both ii-para, one having a history of abortions besides, the amount of elastic tissue was extreme, not less than in some of our cases of vii-para or ix-para. There are possibly individual variations in this structure which do not depend upon age and parity.

Some comments are due the condition of the blood vessels. In the bleeding as well as in the non-bleeding group, there was a most constant change in the blood vessels of aged and multiparous women. No exceptions were seen to this rule. We have found unlike the majority of authors, but in accord with Wittek, the intima participating to some extent in the thickening of the blood vessels in a few cases only.

EXPERIMENTAL WORK

To our regret we did not have at our disposal the ovaries for study and we cannot express our views upon the significance of persistent follicle cysts and absence of fresh corpora lutea in cases of irregular uterine bleeding. But we can say that there was a remarkably frequent association of ovarian pathology of any kind (small serous cysts, follicle cysts, ovarian fibroid) with cases of uterine bleeding. This fact and also the frequency with which the cure is effected either by surgery of the ovaries or by the use of radium and X-rays is sufficient to arrest one's attention to the ovarian influences upon uterine hæmorrhages.

When the study of the cause of irregular uterine bleeding was in its infancy there was a vague knowledge of the relationship between the function of the ovaries and hyperplastic uterine mucosa accompanied by uterine hæmorrhages.

As early as 1882, Brennecke suspected the ovary. According to this author the thickened mucosa in some of the cases of uterine bleeding is in a state of hyperplasia which is due to ovarian influences: he proposed to call this form "endometritis hyperplastica ovarialis." Pankow, in 1909, attributed the cause of irregular uterine bleeding to a possible congestion of the ovaries or to any disturbance of their function. Poelzl, in 1912, was one of the first to point out with precision the departure from normalcy which she found in the ovaries in cases of irregular uterine bleeding. In 4 cases of atypical uterine bleeding in young women she observed a cystic degeneration of the ovaries (*kleinzystische Degeneration*), nowhere were seen fresh corpora lutea, and in

3 of these 4 cases the endometrium was thickened and hyperplastic. She believed that there is a causative relationship between the ovarian changes and the uterine bleeding. Schroeder, in 1915 and 1919, gave the most impressive evidences in favor of the ovarian theory of uterine bleeding. The author believes that the cause of that variety of uterine bleeding which has no discernible clinical signs and which he calls "metropathia hæmorrhagica" lies in the ovaries. In all his series the mucosa was found in a state of pathological proliferation. In all cases, in which the adnexa were available for study, the ovaries showed persistent follicle cysts and absence of fresh corpora lutea formation. Schroeder considers that the follicle fluid exerts an influence upon the endometrium and causes its hyperplastic condition. Novak, Novak and Martzloff, Babes, Wilfred Shaw, and others supported in main the ovarian theory of functional uterine bleeding. However, not all observers have invariably found persistent follicle cysts and lack of fresh corpora lutea in the ovaries.

From our material we are not in a position to say with precision in what condition the graafian follicles and the corpora lutea were found, as we ourselves did not study the ovaries microscopically. We wish to point out that although very frequently pathological changes in the ovaries were found in cases of uterine bleeding, nevertheless not infrequently the same type of pathology was seen in the non-bleeding group. If it is true that in our series 60 per cent in the bleeding group showed ovarian abnormalities, it is also true that in the non-bleeding group 42 per cent of inspected adnexa revealed alterations in the ovaries. If the future should disclose the ovaries as the main cause of uterine bleeding, that discovery might be due to the new methods of biochemical investigations. We doubt whether the histopathology of the ovary alone would clarify the question to a greater extent than the histology of the uterus did, but we are inclined to believe that experimental studies of the gonads may throw some light upon this obscure cause of uterine bleeding.

Having in mind the idea that the ovarian misfunction and hyperfunction could be responsible for uterine bleeding, we attempted to inject into animals the female sex hormone in order to detect any possible alterations in the uterine structure. We did not discriminate between the source of origin of the ovarian hormone for we were under the impression that various kinds of oester-producing female sex hormone act similarly upon the uterine mucosa and sexual life of the animal (Frank). What we actually wanted was to see whether prolonged hyperæmia incidental to hyperfunction of the uterus would produce fibrosis and whether prolonged action of the female sex hormone is capable of creating an histological picture similar to "hyperplasia endometri" (pathological entity). For our experiments we chose dogs, rabbits, and guinea pigs. The dog and the rabbit proved animals too big for the amount of material used, therefore, in our later work we confined ourselves to experiments on guinea pigs only. Young, virginal guinea pigs were injected with oester-producing hormone "amniotin" (Squibb). One-half cubic centimeter, which contained 10 Allen-Doizy units, was injected subcutaneously every other day until 15 doses were given. The injection we began on the fourth day after a laparotomy removing the right horns of 2 animals. A month later we removed the left horns of the same animals and after sectioning and staining compared the histological picture with the right horns. Only mild changes were observed in the uterine mucosa and none whatsoever in the mesometrium. We did not see any alterations in the stroma of the endometrium, but some of the glands in the injected animals showed signs of activity. The epithelium of the glands became more transparent and taller and irregularly arranged at some areas. The lumina of these glands were filled with a mucoid substance. We tested the potency of "amniotin" by the Allen-Doizy vaginal smear test and we found it mildly active, that is to say that the vaginal smear revealed a preponderance of epithelial cells, but these were mostly nucleated. In view of the fact that commercial products are not suitable for experimental work and also that we were not in a position at that time to produce the hormone in our laboratories, we discontinued the experiments

Fig. 1. Specimen 641. Patient was a i-para of unknown age. The endometrium appears to be moderately hypertrophic and hyperplastic. A distinct endometrosis is observed at a short distance from the mucosa. Hematoxylin eosin stain.

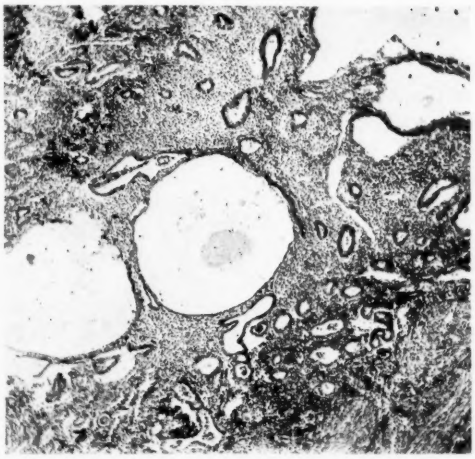

Fig. 2. Specimen 5606. From a multipara (the exact parity not known) of 55 years. This specimen reveals large cystic glands in the endometrium, the rest of which does not show signs of hyperplasia. The glands of the mucosa are rather narrow, epithelium of normal appearance, the stroma varies in density, the cysts are lined with low cuboidal and flattened epithelium, their cavities contain amorphous débris. Hematoxylin eosin stain.

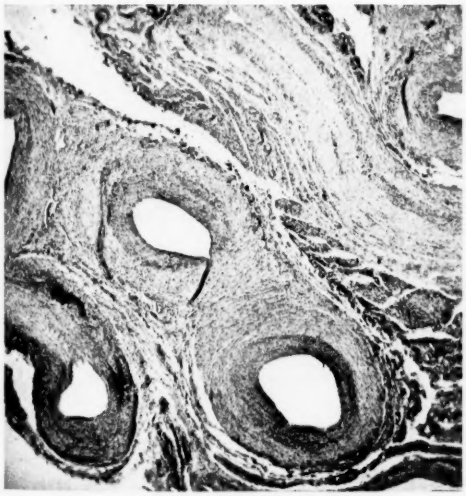

Fig. 3. Specimen 5734. In this instance parity was not known. The patient was 55 years old. In this section the thickened blood vessels are seen very distinctly. In one of the arteries there are calcified areas seen as dark blue spots. A large vein is shown extremely thickened with the lumen reduced to a slit. Hematoxylin eosin stain.

Fig. 4. Specimen 5604, from the bleeding group. The parity is not known, patient's age was 63 years. This specimen demonstrates distinctly the participation of the intima in the thickening of the blood vessels. There is a large amount of elastic tissue within the mesometrium, which appears as intensely dark stained, coarse bands and clusters. The internal elastic lamina is thickened and uneven. Weigert stain for elastic tissue.

on animals and limited our interest to the clinical material. We do not know whether another more potent product would cause any alterations in the mesometrium and endometrium. But we do know that "amniotin," in the dosage used, was not sufficiently efficacious to produce the expectant pathological picture, except mild degrees of pro-oestreal changes. Before we can draw conclusions as to the ability of the oester-producing female sex hormone to cause changes other than pro-oestreal, more potent products should be used in a larger number of animals.

SUMMARY AND CONCLUSIONS

1. Hyperplastic and hypertrophic conditions of the endometrium were seen in the bleeding group as well as in the non-bleeding but with more frequency in the first one.

2. Cystic glands of the mucosa were observed in hyperplastic endometrium frequently, but not as a rule. Occasionally a normal mucosa showed the same cystic transformations. Cystic endometrium was met with in the non-bleeding as well as in the bleeding group of cases.

3. Fibrosis uteri was observed in both groups, but more often and to a higher degree in the bleeding variety.

4. No essential difference in the condition of the blood vessels has been noted in these two groups, these changes, fibrotic in character, occurred most frequently in aged and parous women (the dependence from these conditions is not absolute).

5. No difference in the amount and distribution of elastic tissue was seen in the uteri of these groups, the variations depended upon parity largely and to some extent they were individual in character.

6. On no occasion was an inflammation of the myometrium seen.

7. A departure from a normal condition of the ovaries was seen in the bleeding cases more frequently than in the non-bleeding group. In about the same proportion mild chronic salpingitis could be detected in specimens of both groups.

8. There is no single feature or a combination of features, which is pathognomonic of idiopathic uterine bleeding.

I wish to thank Dr. I. Pilot for his co-operation and generous assistance in conducting this work.

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TOXIC NEURONITIS OF PREGNANCY

A Clinicopathological Report

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THAT infections, trauma, and pressure upon nerves during pregnancy may produce paralysis is well known, but it is not well recognized that paralysis may result from some form of autointoxication during pregnancy. Textbooks on neurology and obstetrics discuss briefly, if they mention at all, the existence of such a complication. Even the most recent monographs and critical reviews dealing with toxæmias of pregnancy fail to include polyneuritis or neuronitis with other complications, such as eclampsia, chorea of pregnancy, and pernicious vomiting. It is true that paralysis from toxæmia of pregnancy is seldom encountered, but the existence of such a paralysis has long passed beyond the stage of doubt. It is likely that its presence will be less frequently overlooked when the attention of the profession has been sufficiently directed toward it.

The nerve involvement with which this paper will deal occurs usually in the early part of pregnancy and usually follows uncontrollable vomiting. Cases of paralysis occurring after delivery will not be included in this report. With our present knowledge, it is difficult to be sure that toxic changes appearing in the nervous system after delivery are of the same or similar origin as those appearing during pregnancy. The occurrence of infection and local injuries to the sacral plexus is so common that it is difficult to rule out these possibilities in many instances. In most cases of postpartum paralysis elevation of temperature and absence of hyperemesis have been reported. In consideration of these facts, cases of paralysis occurring after delivery will not be included in this report.

Up to the latter part of the nineteenth century, cases of paralysis associated with pregnancy have appeared sporadically in the literature by Gamet, Abeille, Colombet, and others, but insufficient data accompanying them and indefinite clinical and laboratory findings prevented the condition from being recognized as a definite entity. Jolly published in 1885 reports of 2 cases which may be regarded as a presentation of paralysis due to a toxic condition arising during pregnancy, although he believed the paralysis to be of a functional origin. Four years later a committee of the French Academy of Medicine (12) reported on a case presented by Desnos, Joffroy, and Pinard. The committee thought the paralysis was due to a reflex action from the uterus. The same year, Whitfield reported the first case in the English literature. Since then cases have appeared more frequently. In 1904–1905, Hoesslin published an extensive monograph describing 493 cases of paralysis associated with pregnancy. In this paper he included all types of paralysis, independent of and dependent upon pregnancy, and regarded 46 of them directly due to autointoxication either before or after delivery.

Although a rather large number have been reported in the literature as toxic nerve changes of pregnancy, critical examination of the records revealed obvious errors in diagnosis in some, and in others the data were insufficient to exclude the possibility of neurological changes having developed from exogenous infections or other sources. After eliminating all of such questionable cases we were able to collect 52 in which we believe the neurological changes were dependent upon pregnancy. We, ourselves, have had the opportunity of observing 4 more cases. Three of these died and a postmortem examination was made on each. The fourth patient recovered.

REPORT OF CASES

Case 1. M. S., married, aged 29 years, was brought to the University Hospital on a stretcher on October 2, 1926. Her family history was negative. She was a college graduate and had taught school up to the onset of her present illness. She had had two attacks of hysterical aphonia precipitated

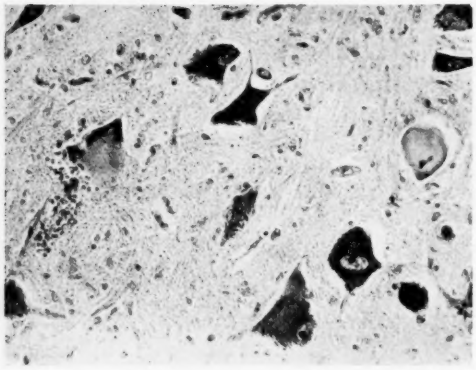

Fig. 1. Case 1. Anterior horn cells in the lumbar portion of the spinal cord. Thionin stain. Photomicrograph showing swelling of cells, loss of Nissl substance, and eccentricity of nuclei. In the left central portion of the field is a cell undergoing necrosis and partially surrounded by a small petechial hæmorrhage.

while she was under a nervous strain teaching young children parts for church plays. In both instances she recovered within a few weeks. Her history as to venereal diseases and exposure to drugs was negative. Eighteen months after her marriage she became pregnant for the first time. Five or 6 weeks later, she began to have emesis. This condition gradually grew worse, until nothing could be retained. The vomitus was green and bitter and frequently blood tinged. Nausea frequently accompanied it. She lost about 40 pounds in weight and became very weak. About 10 weeks later (September 7, 1926) the vomiting stopped rather abruptly.

At the time her vomiting ceased, she complained of paralysis in her feet which gradually ascended her limbs. Mental symptoms also appeared about the same time. She became "absent-minded" and forgetful. About 1 week after onset of the motor paralysis, she complained of numbness in her feet and hands. She became restless and slept poorly, and was apprehensive and afraid. Frequently she remarked that she "might fall out of bed and injure the baby." Shortly afterward she lost control of her bladder and bowels. She developed a staring expression, and she lost her ability to speak above a whisper. Her family physician thought she was having another attack of hysteria and brought her to the hospital for further study.

Physical examination. The patient was markedly undernourished and showed marked signs of recent weight loss. The pulse was 120, temperature 98.6 degrees, respirations 32 per minute. Blood pressure was 110–70. She was restless and tossed about in bed, although she had flaccid paralysis of the extremities and was unable to sit up alone. She talked in a husky whisper. She had a wild, staring expression. Her lips and fingers were cyanotic. Exophthalmus was present and there was a definite lid lag. The thyroid was not enlarged. The respirations were costal in type, and the abdomen would sink instead of rise with each inspiration, suggesting paralysis of the diaphragm. The breath sounds were markedly decreased in the lower parts of the chest. There was dullness on percussion below the fourth interspace. Except for tachycardia and occasional extra systoles the heart was normal. The breasts were enlarged and areolæ were present.

Neurological examination. The eye grounds showed pale retinæ, blurred and indistinct disc margins, and slightly enlarged veins, indicating optic neuritis. The pupils reacted to light and accommodation. Extraocular muscle movements were normal. Corneal and pharyngeal reflexes were absent. She had difficulty in swallowing at times but the uvula would elevate in the midline upon phonation. Examination of the vocal cords showed no definite abnormality. The biceps and triceps reflexes were equal but decreased. The abdominal reflexes were absent. The knee and ankle jerks could not be elicited. No plantar response was obtained upon stimulation of the soles of the feet. There was marked weakness of the extremities, more pronounced in the distal portions. There was definite atrophy in the lower extremities with slight contracture at the knees. The patient was unable to raise her legs from the bed and she could not sit up alone. She gave variable and inconsistent responses to cotton and pin prick, but there appeared to be definite hypæsthesia and hypalgesia in the arms and legs, most marked distally. Deep muscle and tendon pain were increased. She had difficulty in starting urination and had incontinence at other times.

Mental. The patient tried to co-operate but her responses suggested a cloudy sensorium. She appeared worried and anxious about her condition. Her face suggested fright. Her memory was poor for recent and remote events. She thought she was in Texas because her mother who recently came from Texas was at her bedside. When asked what year it was she said, "I think 1923." She thought it was the month of August when it was October, 1926. She realized that she could not think or reason so well as she could prior to her illness.

Laboratory data. The hæmoglobin was 88 per cent; red cells 4,270,000; white cells 11,000 with polymorphonuclear cells 65 per cent. The urine was dark amber in color; specific gravity 1.027; albumin negative; many pus cells and epithelial cells were present. The blood urea nitrogen was 10.73; creatinine, 1.74; blood sugar, 120 milligrams per 100 cubic centimeters. The blood Wassermann test was negative. The spinal fluid report was as follows: normal pressure, color, clear; 1 cell per cubic millimeter; Nonne, negative; Noguchi, negative; Wassermann test, negative; colloidal gold, 0011100000. Nose and throat cultures were negative.

On the second day of hospitalization, October 3, 1926, a basal metabolism test was taken to rule out hyperthyroidism. The rate was −3 per cent although she co-operated poorly. Fluoroscopic examination of

the chest showed paralysis of the diaphragm and atelectasis of the lower lobe of the right lung.

On October 10, 1926, it was noticed that pulse was growing weaker and more rapid, rising to 140 at times. The paralysis was growing more severe and a vaginal hysterotomy was recommended. The operation was performed under caudal anæsthesia. A macerated fetus about 3½ to 4 months old was delivered. During the completion of the operation the patient went into shock, her pupils dilated, and her pulse and respiration gradually failed. She died on the operating table.

Diagnosis. (1) Toxic peripheral neuritis and myelitis of pregnancy; (2) therapeutic abortion.

Autopsy was done 1 hour after death. In the pelvis was found 250 cubic centimeters of blood, the obvious source of which was a recently sutured operative incision in the anterior wall of the cervix and anterior peritoneal cul-de-sac. The liver and kidneys showed a moderate degree of cloudy swelling, but their weights were well within normal limits. None of the other organs were abnormal in even the slightest degree. Gross pathological changes were entirely lacking in the brain, spinal cord, and peripheral nerves.

Histological study. About the centers of the lobules of the liver was a minimal amount of fatty metamorphosis. The cells of the convoluted tubules of the kidneys showed moderate swelling and granular degeneration of their cytoplasm. All other organs of the abdominal and thoracic cavities were normal. The thyroid gland was normal.

In the lumbar portion of the spinal cord there was advanced chromatolysis of the anterior horn cells (Fig. 1). In the larger number of these cells distinct Nissl bodies were entirely lacking, and the cytoplasm was stained a dirty blue. Many of the cells were greatly swollen and almost spherical in shape. Nuclei were frequently eccentric, and occasionally even protruded, in part, beyond the margins of the cell body. The characteristic staining reactions of some cells were lost. The irregularity in outline and structure of these cells made it obvious they were in the early stages of necrosis. In both the gray and white matter of this portion of the cord were a number of tiny fresh petechial hæmorrhages. No inflammatory lesions were found, however, either in the cord or its meninges at this level. The glial tissue and blood vessels seemed entirely normal, and there was no evidence of tract degeneration. In one section taken from the thoracic portion, a small inflammatory lesion was found in the pia arachnoid. This consisted of mild proliferative changes in the fixed connective tissues, and infiltration by a few lymphocytes and mononuclear wandering cells. There were no changes in the nerve cells at this level, and no hæmorrhages were found. The cervical portion was without histological changes. Careful search of the brain failed to reveal pathological changes by any method of study. Marchi preparations of the left femoral nerve and the phrenic nerves revealed outspoken degeneration of large numbers of fibers (Fig. 2). Fat droplets were numerous and large, and in many portions the neurilemmæ of the affected fibers were collapsed and empty. There were no proliferative or exudative changes in any of the nerves examined.

Fig. 2. Case 1. Left femoral nerve, proximal portion. Marchi stain. Photomicrograph showing degeneration in a large number of nerve fibers.

Case 2. N. W., married, aged 28 years, entered the University Hospital September 16, 1929. Her family history was essentially negative. She completed the sixth grade in common school and then left school to help work on her parents' farm. She was considered to be emotionally unstable, easily excited and worried about trifling matters. She married at the age of 20 years. One year later she became pregnant. She had severe vomiting beginning about the sixth week and entered a hospital 2 weeks later. She was not given anything by mouth but was given nourishment by rectum. Twelve days later the vomiting was controlled and she returned home. She complained of some pains in her legs but she was not examined neurologically. She then continued through her pregnancy and delivered a normal child at term.

She became pregnant for the second time about April 15, 1929, and began to vomit about May 10, 1929. Her vomiting became so severe that she was forced to enter a hospital at her home town the latter part of that month. The vomitus was blood tinged at times. She remained at the hospital for about 1 week and then returned home. Again she began to vomit and was sent back to the hospital, where she was treated about 10 days. She improved and returned home, but her vomiting again became severe. Two weeks later she returned to the hospital for the fourth time, where she remained for a period of 5 days. She was then discharged but she was obliged to return to the hospital for the fifth time 2 weeks later. At this time she was pregnant about 3 months. She began to complain of numbness in the lower extremities and she continued to vomit. The physician noticed weakness and tenderness in the lower limbs.

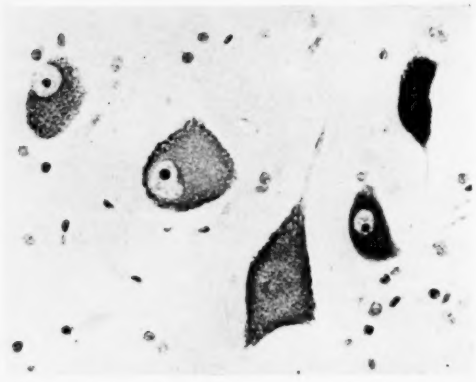

Fig. 3. Case 2. Anterior horn cells in the lumbar portion of the spinal cord. Thionin stain. Photomicrograph showing swelling of the cells and loss of Nissl substance. The nuclei of two of the cells are eccentrically placed.

A few days later the patient could barely move her legs. Four weeks later, August 21, 1929, the patient had a spontaneous abortion. The intensive vomiting ceased 4 or 5 days thereafter, and there was no further vomiting. About September first she developed incontinence and became confused and extremely forgetful. On September 8, she began to show signs of improvement. She was able to move her legs a little, but she could not move her arms. She also had difficulty in swallowing. Because of the patient's peculiar syndrome, the physician referred her to the University Hospital.

Physical examination. The patient was emaciated and anæmic in appearance. Her voice was hoarse and weak. Her temperature was 98.6 degrees and her pulse ranged from 90 to 120 per minute. Her respiration was labored. The blood pressure was 108–76.

Neurological examination. The eye grounds showed evidence of optic neuritis. The discs were slightly raised and the margins were blurred. A small flame-shaped hæmorrhage was seen below the left disc margin. The pupils reacted to light and accommodation. There was a rapid nystagmus when the patient looked laterally. The extraocular movements were normal. The patient had some difficulty in swallowing. The tongue was protruded in the midline, but its strength was decreased. All deep reflexes were absent. The intercostal muscles and the diaphragm were paralyzed. The abdominal reflexes were absent. There was severe weakness in the extremities, more marked in the distal muscular groups. The patient could barely raise her extremities from the bed. The muscles were atonic and atrophic. Because of her marked weakness, coordination could not be tested. The sensory examination was very unsatisfactory because of the poor mental condition of the patient. There appeared to be a decrease in superficial sensation in the hands and in the feet. Muscle and tendon pain sensation was increased.

Mental. The patient was disoriented as to time and place. She thought it was the month of June when it was September. She cried easily and could not give any account of her present illness. She insisted that she was at her friend's home the previous day whereas actually she had been in the hospital for several days.

Laboratory data. A catheterized urine specimen was amber in color; acid in reaction, no sugar; 2+ albumin and many white cells. The hæmoglobin was 38 per cent; red cells 2,090,000; white cells 4,800 with 76 per cent polymorphonuclear cells and 14 per cent lymphocytes. The blood smear showed evidence of a marked secondary anæmia. The spinal fluid was clear, pressure normal; one to two cells per cubic millimeter; negative Wassermann; negative globulin test and negative colloidal gold curve. The blood sugar was 100 milligrams per 100 cubic centimeters and the blood urea nitrogen was 9.33 milligrams per 100 cubic centimeters.

The patient had difficulty in breathing and swallowing. The second day in the hospital, the temperature rose to 102 degrees and the pulse rate increased to 130 per minute. Numerous râles were heard in the chest. X-ray examination of the chest showed evidence of congestion. The patient died on the third day of residence (September 19, 1929).

Diagnosis. (1) Toxic neuronitis of pregnancy. Bronchial pneumonia.

Autopsy was done 4 hours after death. Both lungs showed a mild hypostatic congestion without pneumonia. The liver was definitely enlarged. It weighed 2000 grams, was considerably paler than normal, and its cut surfaces were cloudy. There were no focal lesions. The gall bladder contained a number of faceted calculi, but its walls were not abnormally thickened. Each kidney weighed 170 grams. Both were swollen and pale, and their cut surfaces were cloudy. All of the other viscera, including the brain and spinal cord, were normal.

Histological study. In the lungs was found a purulent bronchitis without pneumonia. The liver showed a slight swelling of the hepatic cords, and occasional cells showed fatty changes. In the portal spaces were occasional small aggregations of lymphocytes. There were no areas of necrosis. There was slight swelling and granular degeneration of the tubular epithelium of the kidneys, but the glomeruli were normal. The uterus and all other abdominal and thoracic viscera were normal.

In the lumbar portion of the spinal cord, the anterior horn cells showed severe chromatolysis, with disappearance of Nissl bodies (Fig. 3). These same cells were swollen, and their nuclei were frequently eccentric. In none of the cells were there evidences of necrosis. No hæmorrhages were found, and there were no evidences of inflammation. Sections taken from the thoracic portion of the cord revealed no pathological changes, while in the cervical portion the anterior horn cells showed alterations similar to

those in the lumbar segment, but somewhat less marked. In the entire cord no evidences of nerve tract degeneration could be demonstrated, and the spinal meninges were normal. In the medulla oblongata, early chromatolytic changes were found in the hypoglossal nuclei. In the left lenticular nucleus was a solitary, small vessel surrounded by a collar of lymphocytes. In the region of the right superior frontal gyrus were found mild proliferative changes about a number of subcortical vessels (Fig. 4). About the same vessels were infiltrations of phagocytic mononuclear cells containing granules of blood pigment. Careful search of all other portions of the brain failed to reveal other pathological changes. Evidences of degeneration in peripheral nerves were minimal, and even questionable in Marchi preparations. By the Bielschowsky method, fragmentation and granular degeneration of neuraxones were demonstrated in the phrenic nerves.

CASE 3. E. S., married, aged 30 years, was brought to the Minneapolis General Hospital December 30, 1929, in a moribund condition. She was extremely toxic and weak. The patient had always been of a very nervous temperament. She had had frequent temper tantrums in her childhood. She did not get along with her parents and left her home when she was about 15 years old. She had one sister and an aunt in a State Hospital for the Insane. She married in 1921. She had two daughters, aged 7 and 3, and one son aged 5. Four years ago she became pregnant for the fourth time, but she had a spontaneous abortion in the fifth month. About 2½ years later she again became pregnant but after taking some chemical abortifacients she aborted in the fourth month.

Her sixth and last pregnancy began in August, 1929. About the seventh week she began to vomit; she went to a physician who was unable to control the vomiting. She tried to produce abortion by using both chemical and mechanical means on several occasions, but she was able to produce only a slight hæmorrhage. She was forced to remain in bed the first week in November because of weakness. She called another physician who stopped all food by mouth and fed her by rectum. Her pulse was about 130 beats per minute and her temperature was 99 degrees. Her urine was normal. The vomiting persisted until December 15, 1929. At the time the vomiting ceased, the patient became confused and complained of severe pains in her legs and she developed incontinence of the sphincters. She was admitted to the General Hospital December 30.

Physical examination. The patient was dehydrated, delirious, restless, and unco-operative. The right eye was blind. There was a colombona of the iris and an absence of the lens in that eye. The respirations were rapid and labored. The temperature was 102 degrees. The diaphragm was paralyzed and the patient used the accessory muscles of respiration. The blood pressure was 142–94. The fundus of the uterus was about two finger breadths below the umbilicus.

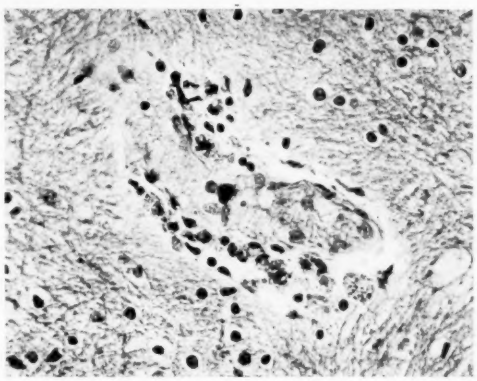

Fig. 4. Case 2. A small blood vessel in the right superior frontal gyrus. Hematoxylin-eosin stain. Photomicrograph showing a number of mononuclear phagocytic cells containing granules of blood pigment about a small blood vessel.

Neurological examination. The ophthalmoscopic examination of the right eye showed an old optic atrophy due to the congenital defect of that eye. The left eye showed optic neuritis with small, fresh hæmorrhages in the retina. The left eye reacted to light and accommodation. The rest of the cranial nerves were negative. The biceps and triceps reflexes were normal. The abdominal, patellar, hamstring, and ankle reflexes were absent. The diaphragm was paralyzed. There was marked weakness of the extremities, especially in the lower limbs. Muscle and tendon pain sense was increased.

Mental. The patient was disoriented and delirious. She was unable to answer questions or to cooperate in the examination.

Laboratory data. The specific gravity of the urine was 1027. There was a faint trace of albumin and no sugar. There were four pus cells per high power field in the centrifuged specimen, but no other formed elements. The hæmoglobin was 65 per cent. Erythrocyte count 3,500,000; leucocyte count, 8,100; with 80 per cent polymorphonuclears. The spinal fluid was clear, the globulin test was negative, and the pressure was normal. There were no cells. The Nonne and Wassermann tests were negative. The blood urea nitrogen was 7.2 milligrams per 100 cubic centimeters and the blood sugar was 680 milligrams per 100 cubic centimeters (after intravenous glucose). The carbon dioxide combining power of the plasma was 53 per cent.

The patient did not respond to vigorous forcing of fluids and intravenous glucose. Her pulse and temperature continued to rise and she died on the third day in the hospital.

Diagnosis. (1) Toxic neuronitis of pregnancy; (2) bronchial pneumonia.

Autopsy was performed 1 hour after death. The positive gross findings at autopsy were mild œdema

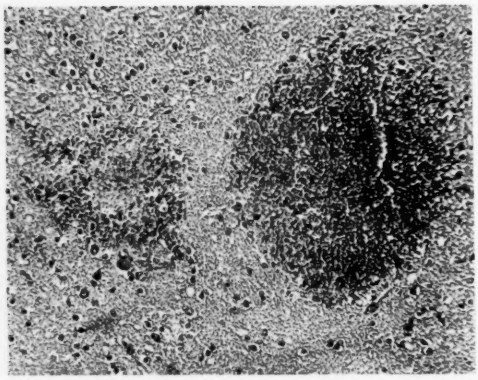

Fig. 5. Case 3. The right mammillary body. Hematoxylin-eosin stain. Photomicrograph showing two fresh petechial hæmorrhages.

of the lungs with hypostatic bronchopneumonia, slight swelling and cloudiness of the liver and kidneys, and enlargement and softening of the spleen (320 grams). The spleen culture resulted in a growth of bacillus coli communis. This organism was regarded as a contaminant. All other organs were entirely normal. The uterus contained a normal 4 months old fetus with membranes intact. There were no gross changes in the central or peripheral nervous system.

Histologically the bronchopneumonia was confirmed, and in addition, a moderately severe exudative cystitis was found. There were no lesions in the liver, spleen, kidneys, uterus, thyroid gland, or adrenals. In the placenta were found occasional thromboses of small vessels, with infarction of villi, but there was no evidence of primary inflammatory change.

In the lumbar and sacral portions of the spinal cord there was a moderate degree of chromatolysis of the anterior horn cells. This change, though distinct, was not marked. Swelling of these cells was only slight, and there was no nuclear eccentricity. Similar, but even less marked lesions were found in the cervical portion of the cord. In the thoracic portion no changes could be demonstrated. In no portion of the cord or its coverings were there hæmorrhages, inflammatory changes, or evidences of vascular disease.

In the brain there were more conspicuous lesions. Both mammillary bodies contained large numbers of petechial hæmorrhages (Fig. 5). There were similar petechial hæmorrhages in the anterior central gyrus, the medulla oblongata, and in the pons near the floor of the fourth ventricle. All of these hæmorrhages were quite fresh, hæmoloysis not yet having taken place. None were associated with inflammatory changes or demonstrable vascular disease. In the white matter of the left anterior central gyrus, a small collection of lymphocytes was found about one vessel. The giant pyramidal cells of the anterior central gyri showed the changes of early chromatolysis. A number of small lesions were found in the meninges. Over the right anterior central gyrus a small area of the pia arachnoid was thickened and contained a number of mononuclear phagocytes and occasional plasma cells. Over the middle frontal gyrus similar but less marked changes were found. In the meninges overlying the right superior occipital gyrus there was a diffuse infiltration of mononuclear phagocytes, most of which contained blood pigment. No peripheral nerve lesions could be demonstrated in hematoxylin and eosin or Marchi preparations. Bielschowsky preparations revealed degenerative changes in occasional neuraxones of the sacral plexus.

Case 4. L. P., married, aged 24 years, entered the University Hospital January 27, 1930. Her past history was essentially negative. She finished the grade school and worked in a watch factory for 5 years. She married in 1928 and became pregnant for the first time October 25, 1929. She began to have nausea and vomiting about 4 weeks later. Vomiting became so severe that hospitalization was necessary. She improved for one week and returned home. She again vomited frequently and was admitted to the University Hospital January 27, 1930. Exclusion of visitors, large doses of sodium bromide, intravenous glucose, and abstinence from food by mouth failed to control the vomiting. On February 11, 1930, she talked irrationally and complained of pain in her legs. Three days later an abortion was advised because the patient's condition was growing critical. She complained of diplopia and she was very restless and confused. On February 14, 1930, the uterus was packed. The following day her condition grew so critical that immediate intervention was necessary and the fetus was removed piecemeal.

Physical examination. The patient showed evidences of marked recent weight loss. February 17, 1930, her pulse was 120 per minute. The blood pressure was 126–86. There was dullness on percussion over right chest. Except for tachycardia the heart was normal. The abdomen was flaccid.

Neurological examination. The ophthalmoscopic examination showed large hæmorrhages in the retinæ. The optic discs were reddened and the margins were blurred. The patient complained of diplopia but the extraocular movements were normal. The rest of the cranial nerves were normal. All of the deep reflexes were absent. The arms and legs were weak and they showed definite atony and atrophy. The weakness was most marked in the distal muscle groups. The diaphragm was paralyzed. The sensory examination was difficult to evaluate for the patient was resistive and unco-operative. She cried upon the least stimulation. There appeared to be marked increased in the muscle and tendon pain sense in the lower extremities.

Laboratory data. The urine contained diacetic acid and acetone but was negative otherwise. The blood showed 47 per cent hæmoglobin with 13,700 leucocytes per cubic millimeter. The blood urea

nitrogen was 14.47 milligrams per 100 cubic centimeters and the blood sugar was 80 milligrams per 100 cubic centimeters. The blood Wassermann test was negative. Nose and throat cultures were negative. X-ray examination of the chest showed massive atelectasis of the right lung. The carbon dioxide combining power of the plasma was 48 per cent.

A few days after the operation the vomiting ceased. The neurological symptoms, however, continued to progress for two weeks. The legs and arms became weaker, and the patient complained of pains in her extremities. About March 1, she began to improve. She became oriented but she had almost a complete amnesia for the events of the previous 2 weeks. She stated that her extremities became numb immediately after the operation but she could not recall what happened for 2 weeks after the operation. The patient was discharged from the hospital in April, 1930. On July 27, 1930, she wrote that she was putting on weight and walked a few steps. Nine months later she returned to the University Hospital and was found to be negative except for some atrophy and slight amount of contractures in her lower extremities. She was able to walk for long distances and had no complaints.

ETIOLOGY

Many divergent suggestions have been offered to explain the etiology of neuronitis of pregnancy. In 1859, Churchill offered anæmia, uræmia, rheumatism, and hysteria as possible causes of the paralysis. Jaccoud (1886) made a highly theoretical suggestion that the paralysis was due to exhaustion of the nervous system by prolonged and continual excitement of the cord, and that the impulses were transmitted by the uterine nerves, exhausting the excitability of that particular segment of the cord and closing the avenues by which motor impulses pass. A little later Jolly ascribed the paralysis to hysteria. Moebius (1887) was one of the first to suggest a theory of autointoxication, a concept which is generally accepted at the present time. He believed that some "morbid condition of the blood" of the pregnant woman was the causative factor. Tuillant, noticing that severe vomiting preceded the neuritis, suggested that the lack of nourishment was the probable cause. To refute this theory, Lindemann undertook a series of observations on dogs, and his results showed that malnutrition alone, however extreme, failed to show any microscopic degenerative changes in nerves. Polyneuritis resulting from starvation has been reported by Schlesinger and others, but histopathological studies have been largely neglected. Inasmuch as the majority of the cases of toxic neuronitis of pregnancy cleared up following the interruption of pregnancy, it appears that the neuritis is not due to inanition. Hassin studied the brain of a man who starved to death. He found no structural changes in the nerve cells or nerve fibers.

Even now the etiology of toxæmia is obscure, as Stander has indicated in a recent monograph "The Toxæmias of Pregnancy." Since 50 per cent of pregnant women have nausea and vomiting in the early part of pregnancy, Bouchard made a statement that all pregnant women suffer to a greater or less extent from autointoxication. Viet held that all disturbances of pregnancy result from cytolytic processes following the entrance of fetal ectoderm into the maternal circulation. Stone, Ewing, and others maintain that vomiting of pregnancy, yellow atrophy of the liver, and eclampsia are all manifestations of disturbed metabolism and should be grouped together under a common heading of toxæmia of pregnancy. But, in the cases we have studied, neuronitis of pregnancy presents a distinct picture, both clinically and pathologically, from the other complications which result from toxic conditions in pregnancy.

CLINICAL PICTURE

The clinical and pathological picture of the nerve changes in pregnancy is the same as that resulting from alcoholism, infectious conditions, and diet deficiency disturbances such as beri beri and pellagra. The diagnosis is made only by careful history and laboratory examination. The exact nature of the toxins producing neuronitis is still unknown. The blood chemistry in this condition is normal but it is realized that laboratory tests for the retention of toxic products are very crude measures of subtle metabolic processes. Cloudy swelling found at necropsy is a finer index of the retention of toxic products than any known laboratory test.

Occurrence. Age has no great significance as is seen in Table II. The condition occurs most frequently between 21 and 35 years, the period when the incidence of pregnancy is the

TABLE I.—SUMMARY OF CASES

Author Year	Age Gravida	Hyperemesis	Motor symptoms				Sensory symptoms	Sphincteric disturbance	Mental symptoms	Additional data	Subsequent history	Termination
			Onset	Type	Distribution	Degree						
Jolly 1885	16 i	1st mo. ++++	4th mo.	L.m.n.	Lower limbs	Marked	Decreased sensation especially on left side		"Hysteria"		Spontaneous abortion at 4½ months	Walked with cane 6 months after abortion
Jolly 1885		1st mo ++++	5th mo.	L.m.n.	Lower limbs	Marked	Lower limbs cold and cyanotic		"Hysteria"		Artificial abortion at 5th month	Improved
Desnos, Joffroy, and Pinard 1889	31 iii	1st mo. ++++	5th mo.	L.m.n.	Marked in right extremities	Moderate	Paræsthesias in extremities		Memory impaired and faculties dulled	Hyperemesis stopped at onset of paralysis	Artificial abortion at 5th month	Improved 1 month after abortion
Whitfield 1889	40 vii	6th mo. ++++	8th mo.	L.m.n.	Upper and lower extremities	Moderate	Numbness in extremities and nerve trunk tenderness				Normal delivery	Rapid improvement after delivery
Polk 1890	27 ii	1st mo. ++++	4th mo.	L.m.n.	Upper and lower extremities	Marked	Tenderness and paræsthesias in extremities	+	"Acute mania"	Vomiting ceased when paralysis appeared	No abortion performed. Died of respiratory paralysis 6th month	Died. Autopsy reported
Kast 1891	35 iv		7th mo.	L.m.n.	Lower limbs and thorax	Marked	Sensory loss below mid thoracic region	+			No abortion performed	Died 7½ months. Autopsy reported
Solowieff 1892	24 i	1st mo. ++++	3rd mo.	L.m.n.	Lower limbs	Moderate	Hyperæsthesia in lower limbs with nerve and muscle tenderness		Cloudy sensorium and delirium	Pulse 130. History of mental disease in the family	No abortion performed	Died 7½ months. Autopsy reported
Stembo 1895	25 i	2nd mo. ++++	3rd mo.	L.m.n.	Lower limbs	Mild	Decreased sensation in lower limbs. Muscle tenderness			Pulse normal	Delivered a normal child at 8th month	Improved after delivery
Eulenberg 1895	27 ii	4th mo. ++++	4th mo.	U.m.n. L.m.n.	Dysphagia, aphonia, and lower limb paralysis	Moderate	Decreased sensation in extremities	+	Melancholy and confused		Artificial abortion at 5th month	Much improved 4 months later
Mader 1895	25 iii	3rd mo. ++++	3rd mo.	L.m.n.	Lower limbs	Marked	Sensory loss in lower limbs	+			Artificial abortion at 5th month, but condition continued to progress	Died 7½ months. No autopsy performed
Elder 1896	33 ix		6th mo.	L.m.n.	Upper and lower limbs	Mild	Decreased sensation in extremities				Normal delivery	Recovered in 4 weeks
Elder 1896	37 xi		6th mo.	L.m.n.	Upper and lower limbs	Mild	Decreased sensation in extremities				Normal delivery	Recovered 4 months later
Reynolds 1897	24 i	1st mo. ++++	5th mo.	L.m.n.	Lower limbs	Marked	No definite sensory loss	+			Artificial abortion at 4th month. Paralysis appeared 1 month later	Much improved in the 5th month
Boissard 1903	22 i	2nd mo. ++++	4th mo.	L.m.n. U.m.n.	Upper and lower extremities	Marked	Decreased sensation in extremities	+		Slight increase of lymphocytes in spinal fluid. Rapid pulse	Artificial abortion at 5th month	Died few hours after abortion. No autopsy

TABLE I.—SUMMARY OF CASES—*Continued*

Author Year	Age Gravida	Hyper-emesis	Motor symptoms				Sensory symptoms	Sphinc-teric disturb-ance	Mental symptoms	Additional data	Subsequent history	Termination
			Onset	Type	Distri-bution	Degree						
Cathala and Trastour 1904	30 iii	1st mo. ++++	4th mo.	L.m.n.	Lower ex-tremities	Moderate	Impaired sensation in extremities. Increased muscle tenderness	+	Irritable and cried easily but not confused	Severe vomiting in previous two pregnancies, and weakness in sec-ond pregnancy. Pulse 120 to 170	Spontaneous abortion at 4½ months	Improved after abortion but never able to walk again
Oettinger 1904	27 ii		2nd mo.	U.m.n. L.m.n.	Hands, feet, and left side of face	Moderate	Impaired sensation in extremities. Increased muscle tenderness				Spontaneous abortion at 7th month. Fetus was dead and emac-erated	Recovered after abortion
Brauer 1904	— xvi		5th mo.	U.m.n. L.m.n.	Vocal cords, dia-phragm, and ex-tremities	Marked	Paræsthesias and hyperæsthesia in extremities	+	Nervous and very irri-table	Nervous and irri-table in all pre-vious pregnancies	Normal delivery	Improved
Hoesslin 1905	29 v		9th mo.	L.m.n.	Lower ex-tremities	Marked	Sensory changes in abdomen and lower limbs	+		Pulse 88	Normal delivery	Recovered
Alexandroff 1907	— i	1st mo. ++++	3rd mo.	L.m.n. U.m.n.	Eye mus-cles. Up-per and lower limbs	Marked	Decreased sensation in extremities, and increased muscle tenderness		Loss of mem-ory and a severe de-lirium (Korsakoff's psychosis)	Optic neuritis in both eyes. Patient was of nervous type previously. Pulse 135	Artificial abortion about the 5th month	Improved after abortion. Some permanent mental changes
Freund 1908	24 iii		7th mo.	U.m.n. L.m.n.	Upper and lower limbs and left side of face	Marked	Mild sensory changes in ex-tremities				Spontaneous delivery at 8th month but con-tinued to grow worse for 4 weeks	Much improved one year later
Funk 1908		1st mo. ++++	4th mo.	L.m.n.	Lower limbs and right arm	Marked	Loss of sensation in lower extremi-ties		"Korsakoff's psychosis"		Artificial abortion at 5th month	Improved
Fruhinsholz 1909	31 ii	1st mo. ++++	4th mo.	U.m.n. L.m.n.	Lower limbs	Moderate	Spontaneous pains in legs		Definite men-tal changes	Rapid pulse	Normal delivery	Improved
Allmann 1909	21 ii		5th mo.	L.m.n.	Lower limbs	Marked	Marked sensory im-pairment below level of chest	+			Artificial abortion at 5th month	Died 6th month. Autopsy per-formed
Dustin 1909	31 ii	2nd mo. ++++	6th mo.	L.m.n.	Lower limbs	Marked	Increased muscle pain in lower ex-tremities	+	Confused and delirious	Pulse 100	Spontaneous abortion at 6th month	Died 4 weeks after abortion. Autopsy performed
Wallich 1910	21 i	1st mo. ++++	3rd mo.	L.m.n.	Lower limbs	Moderate	Impaired vision and sensation in lower extremities		Definite mental changes	Pulse 120	Artificial abortion at 4th month	Improved after abortion
Herrenschmidt, Lepage, and Dufour 1910	—	1st mo. ++++	4th mo.	L.m.n.	Lower limbs	Moderate	Pain in lower ex-tremities	+	Delirious and amnesia	Pulse 130	Artificial abortion at 4th month	Improved after abortion

TABLE I.—SUMMARY OF CASES—*Continued*

Author Year	Age Gravida	Hyperemesis	Motor symptoms				Sensory symptoms	Sphincteric disturbance	Mental symptoms	Additional data	Subsequent history	Termination
			Onset	Type	Distribution	Degree						
Seige 1911	23 i	1st mo. ++++	3rd mo.	U.m.n. L.m.n.	Upper and lower limbs and right side of face	Moderate	Nerve trunk tenderness			Pulse 140	Normal delivery	Complete recovery
Job 1911	31 i	2nd mo. ++++	4th mo.	L.m.n.	Upper and lower limbs and more marked on left	Moderate	Spontaneous pains and increased muscle pain in lower limbs	+	Delirious	Pulse 120	Artificial abortion at 4½ months	Died 6th month. Autopsy performed
Spire 1913	31 v	None	6th mo.	L.m.n.	Upper and lower limbs, and face	Marked	Decreased sensation with trophic changes and spontaneous pains in lower limbs	+		Pulse 120	Artificial abortion at 7th month	Rapid recovery after abortion
Farani 1914	29 viii		8th mo.	L.m.n.	Lower limbs	Moderate	Nerve trunk tenderness			Pulse 106	Normal delivery	Rapid recovery after delivery
Hornstein 1916	24 iii	2nd mo. ++++	3rd mo.	L.m.n.	Upper and lower limbs	Moderate	Decreased sensation in extremities				Delivered normal child at term with low forceps	Incomplete recovery
Albeck 1916	41 iii	1st mo. ++++	5th mo.	L.m.n.	Lower limbs	Moderate	Tenderness in lower extremities		Amnesia and disoriented		Artificial abortion at 5th month. Living fetus delivered	Improvement began 2 weeks after operation
Albeck 1916	22 i	3rd mo. ++++	6th mo.	L.m.n.	Lower limbs	Moderate	Decreased sensation and nerve trunk tenderness in lower limbs		Amnesia and disoriented		Normal delivery	Improved
Albeck 1916	27 i	2nd mo. ++++	3rd mo.	L.m.n.	Lower limbs	Moderate	Decreased sensation in lower limbs	+	Confused, disoriented, and drowsy		Artificial abortion at 5th month. Living fetus delivered	Marked improvement after operation
Albeck 1916	32 iv	1st mo. ++++	3rd mo.	L.m.n.	Lower limbs	Moderate	Decreased sensation and tenderness in lower limbs		Amnesia and confused		Artificial abortion at 4th month	Improved. Marked contractures present
Krupp 1919	42 vii		3rd mo.	U.m.n. L.m.n.	Lower limbs	Moderate	Not mentioned	+			Fetus died at 5th month. Stillborn delivered at 5½ months	Improved after delivery
Krupp 1919	32 ix		6th mo.	U.m.n. L.m.n.	Upper and lower limbs	Moderate	No sensory symptoms		Lethargic and disoriented		Vaginal cæsarean operation performed in 9th month	Improved after operation
Mills 1919	31 iv	1st mo. ++++	4th mo.	L.m.n.	Upper and lower limbs	Marked	Sensation impaired in extremities			Had hyperemesis with previous pregnancies. Artificial abortion each time	Artificial abortion at 3½ months	Improved after abortion
Ely 1922	29 ii	2nd mo. ++++	3rd mo.	L.m.n.	Upper and lower limbs	Moderate	Vision decreased. Sensation impaired in extremities	+	Confused and memory impaired	Severe hyperemesis in previous pregnancy. Pulse 116	Artificial abortion at 3rd month. Paralysis developed 2 weeks later	Gradual improvement but permanent memory impairment

TABLE I.—SUMMARY OF CASES—*Concluded*

Author Year	Age Gravida	Hyperemesis	Motor symptoms				Sensory symptoms	Sphincteric disturbance	Mental symptoms	Additional data	Subsequent history	Termination
			Onset	Type	Distribution	Degree						
Ely 1922	26 i	2nd mo. ++++	4th mo.	L.m.n.	Lower limbs	Moderate	Decreased sensation in lower limbs	+	Confused, disoriented, and emotional	Pulse 110	Artificial abortion at 4th month. Paralysis 2 weeks later	Improved
Ely 1922	— i	2nd mo. ++++	4th mo.	L.m.n.	Fixed pupils, diplopia. Upper and lower limbs	Moderate	Sensation impaired in extremities. Increased muscle pain		Mild delirium and memory impairment	Pulse 120	Patient refused abortion. Premature delivery at 8th month. Child died 24 hours later	Died from exhaustion in 8th month. No autopsy
Ely 1922	36 iv	3rd wk. ++++	3rd mo.	L.m.n.	Lower limbs	Moderate	Sensation impaired in lower extremities		Disoriented and memory impairment	Hyperemesis with previous pregnancies. Nervous breakdown at 30 years. Pulse 110	Artificial abortion at 3rd month	Improved
Cline 1924	20 i	2nd mo. ++++	2nd mo.	L.m.n.	Upper and lower limbs	Moderate	Sensation impaired in extremities	+	Irrational and confused	Retinal hæmorrhages present. Pulse 130	Artificial abortion at 4th month	Improved after abortion
Gobermann 1927	27 i	1st mo. ++++	3rd mo.	U.m.n. L.m.n.	Dysphagia, and lower limbs	Moderate	Numbness and nerve trunk tenderness in lower limbs	+	Confused and forgetful for recent events	Pulse 120	Artificial abortion at 5th month	Grew worse for 3 weeks and then improved
Weille-Halle 1927	37 iii	2nd mo. ++++	4th mo.	L.m.n.	Upper and lower limbs	Moderate	Hyperæsthesia in extremities	+	"Korsakoff's psychosis"	Pulse 84	Normal delivery	Improved after delivery
Ledoux 1929	20 i	2nd mo. ++++	3rd mo.	L.m.n.	Lower limbs	Moderate	Increased deep muscle pain		Irritable, indifferent, and forgetful	Pulse 110	Normal delivery	Improved
Patten 1929	22 i	2nd mo. ++++	4th mo.	L.m.n.	Upper and lower limbs	Moderate	Hyperæsthesia and increased muscle pain in legs		Confused and disoriented		Artificial abortion at 4th month	Improved
Schaeffer 1930	23 ii	1st mo. ++	3rd mo.	L.m.n.	Diplopia, paralysis of vocal cords and lower limbs	Marked	Numbness in left side of face and lower limbs	+	Anterograde amnesia and disoriented	Pulse 120	Artificial abortion at 4th month	Improved
Personal case No. 1	29 i	1st mo. ++++	4th mo.	L.m.n.	Limbs, abdominal and trunk muscles	Marked	Decreased sensation in extremities	+	Confused, restless, and disoriented	Two previous attacks of hysteria. Optic neuritis. Pulse 110	Vaginal hysterectomy at 5th month. Delivered a macerated fetus	Died immediately after operation. Autopsy performed
Personal case No. 2	28 ii	1st mo. ++++	3rd mo.	L.m.n.	Dysphagia, upper and lower limbs	Marked	Increased muscle pain and decreased sensation in extremities	+	Confused and disoriented	Hyperemesis and muscle tenderness following 1st pregnancy. Optic neuritis 2nd pregnancy. Pulse 130	Spontaneous abortion at 5th month	Improved after abortion but died of pneumonia. Autopsy performed
Personal case No. 3	30 iv	1st mo. ++++	3rd mo.	L.m.n.	Diaphragm, extremities, upper and lower limbs	Marked	Increased muscle pain and decreased sensation in extremities	+	Confused and disoriented	Hyperemesis with previous pregnancies. Optic neuritis in present illness. Pulse 130	Patient's condition was so critical that an abortion was not warranted	Died of bronchopneumonia 6 months. Autopsy performed
Personal case No. 4	24 i	3rd wk. ++++	4th mo.	L.m.n.	Upper and lower extremities	Marked	Increased muscle pain and decreased sensation in extremities	+	Confused and irrational	Patient was nervous and high-strung the past few years. Optic neuritis in present illness. Pulse 120	Artificial abortion at 4th month. Fetus removed piece-meal	Rapid recovery following abortion. Slight contractures 1 year later

TABLE II.—INCIDENCE IN RELATION TO AGE

Age in years	Cases	Per cent
14–20	3	6
21–25	14	30
26–30	13	29
31–35	10	22
36–40	4	9
41–45	2	4
Total	46	100

Age not reported in 6 cases.

TABLE III.—INCIDENCE IN RELATION TO GRAVIDA

Gravida	Cases	Per cent
i	19	39
ii	9	19
iii	7	14
iv	5	10
v	2	4
vi	0	0
vii	2	4
viii	1	2
ix	2	4
x to xvi	2	4
Total	49	100

Gravida not reported in 3 cases.

greatest. Table III shows that the disease occurs more commonly in the first and second pregnancies. In this respect it is similar to the occurrence of hyperemesis gravidarium.

Vomiting. The vomiting usually has its onset the first 2 months of pregnancy (Table IV), which is the same time the so called morning sickness makes its appearance. It is generally mild at the onset and indistinguishable from the ordinary type of vomiting which occurs in about 50 per cent of pregnant women. Gradually it becomes more severe and assumes the pernicious form. Not all forms of pernicious vomiting, however, are followed by nerve changes, although their appearance is identical. The vomiting in this condition rarely responds to the usual form of treatment but ceases abruptly when symptoms of paralysis first appear.

Physical findings. The patient is generally dehydrated and emaciated from vomiting. The blood pressure and temperature are not changed, but the pulse rate is accelerated to 120 or more.

Neurological findings. The first symptom of paralysis occurs most frequently in the third and fourth months (Table V). Weakness, numbness, and increased muscle pain, generally in the lower extremities, are the

TABLE IV.—ONSET OF HYPEREMESIS

Month	Cases	Per cent
First	22	55
Second	13	32
Third	3	7
Fourth	1	3
Fifth	0	0
Sixth	1	3
Seventh	0	0
Eighth	0	0
Ninth	0	0
Total	40	100

usual early complaints. Very often, the complaining woman is unjustly thought to be hysterical or malingering in this stage when she is really ill. As the condition progresses, it involves the abdominal muscles, diaphragm, thorax, upper extremities, and in some cases the cranial nerves. In some cases the neurological symptoms are confined to the peripheral nerves, producing the stocking-glove type of anæsthesia, while in others the cord is involved, producing such symptoms as sphincter disturbances (Table VI). Optic neuritis has been reported by some writers and was seen in all 4 of our cases.

Mental changes. About the same time that neurological changes appear, one generally observes definite mental symptoms characteristic of toxic psychoses as shown in Tables I and VI. Korsakow, who is credited with calling the attention of the medical profession to certain mental changes accompanying polyneuritis in alcoholism, reported, with Serbski (32), similar mental changes in polyneuritis of pregnancy. The patient may be delirious, confused, and disoriented, but opportune confabulation is not common (Ely) as in alcoholic neuritis.

Laboratory findings. Urine examination shows no albumin, and the specific gravity is normal. The blood picture is normal unless some complication exists. The blood chemistry is normal. The spinal fluid is commonly negative, although a few writers have noted a slight increase of lymphocytes.

PATHOLOGY

We have been able to find in the literature reports of only 6 cases in which gross and microscopic examinations were made postmortem. These cases were reported by Kast, Lindemann, Polk, Allmann, Dustin, and Job.

TABLE V.—ONSET OF PARALYSIS

Month	Cases	Per cent
First	0	0
Second	2	4
Third	17	33
Fourth	16	31
Fifth	6	11
Sixth	6	11
Seventh	2	4
Eighth	2	4
Ninth	1	2
Total	52	100

TABLE VI.—FREQUENCY OF COMMON CLINICAL SYMPTOMS

	Cases	Per cent
Paralysis	52	100
Hyperemesis	40	76
Mental symptoms	34	68
Sphincter disturbance	26	52
Tachycardia	25	50

TABLE VII.—MANNER OF TERMINATION OF PREGNANCY

Month of pregnancy	Induced abortion	Spontaneous abortion
First	0	0
Second	0	0
Third	3	0
Fourth	10	0
Fifth	13	3
Sixth	0	2
Seventh	1	1
Eighth	0	2
Ninth	1	0
Total	28	8

Normal delivery in 13 cases.

Lindemann described the pathological findings of Solowieff's case. We have had the opportunity of making postmortem examinations, in 3 cases, bringing the number of autopsied cases to 9.

The absence of gross anatomical changes is striking. The thoracic and abdominal viscera are normal or show only cloudy swelling and mild fatty changes in the liver and kidney.

The brain, spinal cord, and peripheral nerves are usually normal. Kast found an area of yellowish softening of the lower cervical portion of the spinal cord which microscopically showed great swelling of the axis cylinders. Dustin found a decrease in size of the larger nerve trunks.

Careful microscopic examination of the nervous system has nearly always revealed definite lesions; but even these lesions were less conspicuous than the severity of the clinical symptoms would lead one to expect. The peripheral nerves were examined in the cases of Dustin, Lindemann, Job and three of our cases. Nerve degeneration has been demonstrated in every one of these cases. Almost invariably degenerative changes are found in the anterior horn cells of the spinal cord. The changes are most marked in the lumbar portion of the cord and consist of loss of Nissl substance, swelling of the cells, eccentricity of the nuclei, and occasionally cell necrosis. These changes were present to some degree in all 3 of our autopsied cases and were reported also by Dustin, Job, and Kast. The anterior horn cells were normal in the cases of Allmann and Polk. In Lindemann's case, the spinal cord was not examined.

Petechial hæmorrhages formed a rather prominent part of the pathological picture in each of our 3 cases. These lesions were found in the spinal cord in Case 1, and in the brain in Case 3. In Case 2 the brain showed evidences of old petechial hæmorrhages. These lesions have not been noted previously. However, Kast and Allmann were the only 2 to examine the brains of their cases besides ourselves. It is possible that more extensive search would reveal petechial hæmorrhages more frequently.

We may conclude that the characteristic lesions of this condition are degenerative changes of the peripheral nerves and anterior horn cells, and petechial hæmorrhages in the brain and cord.

PROGNOSIS AND TREATMENT

The mortality of this condition is about 25 per cent (Table VII). This mortality rate can be reduced considerably, if the presence of toxæmia is recognized earlier, and if pregnancy is interrupted. The high mortality of the writers' 4 cases is probably due to the failure to recognize the presence of the toxæmia early. In all of these cases the diagnosis was considered as being of functional origin, and the patients were treated with the usual symptomatic treatment, such as rest, sedatives, and restriction in diet. The weakness of these patients was attributed by their physicians to the lack of nourishment rather than to actual nerve involvement.

Pregnant women, with hyperemesis, should be repeatedly examined neurologically. As soon as neurological symptoms appear, the case merits careful watching and artificial induction of labor should be considered. Although the majority of patients improve after abortion, some continue to grow worse the following week or two. This is probably due to the fact that toxins still exist in the circulation and continue to affect the nervous system, persisting in the same manner as the toxins from alcohol poisoning. For that reason the physician must act quickly rather than wait until the patient's condition grows critical before intervention is resorted to. Abortion is frequently deferred too long because it is usually unnecessary in most cases of hyperemesis.

Complete recovery from the paralysis does not always occur, because the nerve cells are frequently destroyed. If the paralyzed extremities are not properly treated, contractures frequently develop. As soon as muscle tenderness disappears, active and passive movements should be instituted.

In several cases reported, this condition has reappeared in repeated pregnancies. Because of such recurrence some writers have felt that this condition is identical with multiple sclerosis. The microscopic findings of the autopsied cases, however, show that these two conditions are different entities.

SUMMARY AND CONCLUSIONS

1. Paralysis resulting from toxæmia of pregnancy has been reported under such names as peripheral neuritis, polyneuritis, and toxic myelitis of pregnancy. The name *toxic neuronitis of pregnancy* has been used by the writers, since the nerve cells are involved as well as the peripheral nerves.

2. Forty-eight cases of this condition were collected in the literature, 6 of them having reports of autopsy findings. In addition to these, the writers added 4 of their own cases with autopsy reports of 3.

3. This condition usually develops in the first trimester and is usually preceded by uncontrollable vomiting. The lower extremities are usually involved first. Later the paralysis becomes more extensive. Mental symptoms of a delirious and confusional nature appeared in about two-thirds of the cases. Sphincter disturbances and tachycardia were present in over one-half of the cases. Optic neuritis was present in the 4 cases observed by the writers, although it was mentioned in only a few of the cases collected from the literature.

4. The blood chemistry and urine were negative in all of the reported cases. The gross findings of the autopsied cases also were essentially negative. In the writers' 3 autopsied cases, the liver and kidney showed, microscopically, a mild cloudy swelling. The microscopic study of the nervous system gave findings characterized by degenerative changes of the peripheral nerves and anterior horn cells. Petechial hæmorrhages were found in a number of the sections of the brain and spinal cord.

5. This condition has been attributed to a form of autointoxication. Its appearance is similar to a severe form of the nausea and vomiting (morning sickness) which occurs in about 50 per cent of pregnancies. The weakness of the patient due to paralysis may be easily confused with weakness due to inanition resulting from hyperemesis, and without careful neurological examination the condition may not be recognized.

6. The histories of the cases studied indicate that interruption of pregnancy as soon as definite neurological symptoms appear is the most satisfactory treatment. The mortality of this condition has been about 25 per cent, but it is believed that this figure can be greatly reduced if the condition is recognized and treated early.

7. Although toxic neuronitis of pregnancy is comparatively rare, its serious character demands attention and emphasizes the need of a thorough neurological examination of pregnant women with hyperemesis.

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THE PATHOLOGICAL ANATOMY OF TESTICULAR TORSION

An Explanation of Its Mechanism

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TORSION of the testicle, frequently called torsion of the spermatic cord, has long been recognized as a clinical entity. Its symptomatology has been adequately described, its etiology surmised, and certain of its pathological aspects studied. The condition is caused by a sudden twisting of the spermatic cord which constricts the vessels of the cord causing acute circulatory disturbances of the testis and adnexa. If the twist is not reduced immediately the structures distal to the lesion become gangrenous. If infection does not supervene, the aseptic gangrene is subsequently organized into a mass of fibrous tissue leading to complete disappearance of testicular and epididymal tissue.

The twist may occur either inside the tunica vaginalis, intravaginally, or outside of it, extravaginally. In intravaginal torsion, only the testis and epididymis are affected, while in extravaginal torsion the tunica and its contents are involved. Only a few cases of extravaginal torsion have been reported. It is said to be found in cases in which the testis is arrested during its descent, either within the abdomen or inguinal region. In reviewing the literature of so called extravaginal torsion, it has been found usually in cases in which an incarcerated hernia had been suspected and at operation a congested and swollen, ectopic, undescended testis was discovered. The description of the pathology encountered in the reported cases makes one suspect that the lesion is the result of pressure rather than a true torsion of the spermatic cord. Some of the reported cases have been operated on late, after complete atrophy and fibrosis had taken place, and it has been assumed that torsion had occurred at an earlier date. From the description of the cases of extravaginal torsion in the literature, we are not convinced that real torsion is the etiological factor. Lowsley has stated that to his knowledge there is no reported case of true extravaginal torsion in the literature, except the case of Taylor. From a study of the report of Taylor's case it seems quite possible that it was one of intravaginal torsion.

Young states that extravaginal torsion occurs only when a severe external force tears the undescended testis from its scrotal attachments. In order to make such torsion possible, the loose areolar connections between the external surface of the undescended testis and the surrounding tissues must be broken; especially the connection with its main attachment, the gubernaculum. The trauma necessary to produce such torsion, and the meager unconvincing literature on extravaginal torsion, makes one doubtful as to its actual occurrence. I am, therefore, using the term "torsion of the spermatic cord" for those cases in which no prior traumatic disturbance or ablation of tissues has occurred and where at operation no change in the topographical anatomy is found, except for the actual torsion of the testis and adnexa in their normal anatomical position.

The problems which confronted us in this study were numerous. Can a normal testis be twisted around its axis and if this is not possible, what are the anatomical relations found in cases of torsion? What is the motive force causing the actual torsion and, if a force of such a nature is found, is it possible to demonstrate that it was really this force which caused the testis to become twisted.

I was fortunate in having operated upon a case of torsion of the testis comparatively early, that is, 18 hours after onset. The case has been reported elsewhere (9). At operation an intravaginal twist of the spermatic cord, cutting off the blood supply of the testis and adnexa, was found. These structures were hanging freely in the vaginal sac like a clapper in a bell (Fig. 1B). The twist was held firmly in position and gentle force would

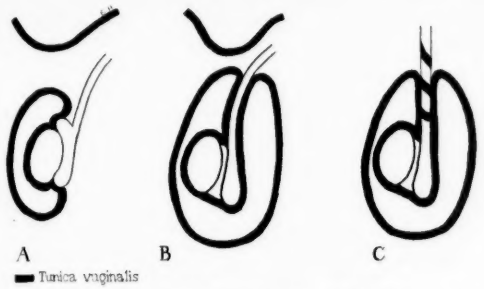

Fig. 1. Vaginal sac in normal and in case of torsion. A, Normal. The tunica vaginalis covers the testis and anterior aspect of the epididymis. B, Torsion case. The tunica vaginalis extends all the way up the cord, covering both testis and epididymis completely. A, Testis and adnexa bulge into vaginal cavity. B, Testis and adnexa hang in the vaginal cavity like a tongue in a bell. C, Illustrating the low extension of the cremaster muscle in case of high investment of the cord, resulting in torsion.

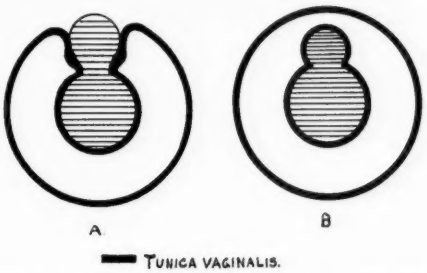

Fig. 2. Cross section of the scrotum in normal and in case of torsion. A, Normal, the posterior aspect of the epididymis is not covered by the tunica vaginalis, but is adherent to the inner wall of the dartos, preventing any lateral movements. B, Torsion case, testis, and epididymis are freely movable in the vaginal sac, making rotation possible.

not reduce it. The earliness of operation which permitted us to obtain an excellent specimen of the infarcted testis, prompted me to study the anatomy and pathology of the lesion by serial histological sections.

On dissecting the normal scrotum, one finds, after the vaginal sac is opened, that it is impossible to rotate the testis markedly around its axis. The reason for this is the strong attachment between the testis and the epididymis, which in turn, is attached to the inner wall of the scrotum. The only possible way to rotate the testis would be to free it from the epididymis by dissection. The normal anatomical situation does not permit marked lateral rotation of the testis, and it is because of this that torsion of the normally developed testis and epididymis is so rare.

In order for the testis to become twisted, it must be freely movable, free from any lateral attachments, and suspended in the vaginal sac by a long stalk of the spermatic cord. Such an abnormality is very rare and one must admit of some disturbance in the normal descent of the testis for this to be present.

During normal descent the testis and adnexa are carried from behind the peritoneal space downward into the scrotum. This is helped by the traction of a guide, the gubernaculum, which, while shortening, brings the organs down into the scrotum and keeps them there by the development of strong surrounding attachments. The tunica vaginalis, an extension of the peritoneum, normally becomes obliterated from its abdominal opening to the proximal portion of the testis. The latter becomes nearly completely covered with peritoneum by invagination, while the epididymis is covered chiefly on its lateral aspect. The posterior portion of the epididymis remains outside of the vaginal sac and is never covered, becoming adherent to the inner wall of the scrotum (Fig. 1A).

In torsion cases, an entirely different situation is found. While the actual descent remains the same, the relations of the organs to the tunica vaginalis are different. During descent, or perhaps after the testis has reached the entrance to the scrotum, the testis and adnexa begin to bulge into the vaginal process. For some reason, perhaps because of a lack of downward pull, this process continues until the tunica vaginalis of the testis completely surrounds the testis and epididymis. When this occurs a portion of the spermatic cord likewise is invested with peritoneum above the testis. The testis, epididymis, and the distal spermatic cord together become an intravaginal body, hanging freely in the vaginal sac. No lateral attachments between scrotum and testis and epididymis are formed. This condition is permanent. The obliteration of the vaginal process of the cord above this, proceeds normally until there remains only the independent vaginal sac of the testis with its visceral and parietal layers, with the

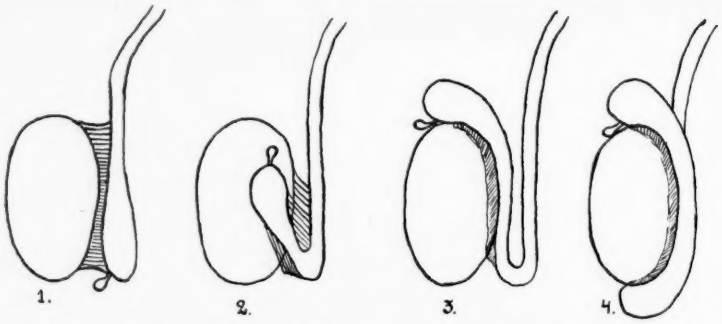

Fig. 3. The physiological rotation of testis and adnexa. Reading from left to right, there is a gradual rotation of the organs *in toto* until final conditions are affected.

organs (testis, epididymis, and part of the cord) suspended in it. This is especially noted in cross sections of the scrotum (Fig. 2) where, instead of only partial investment as in the normal, one finds in the cases of torsion a completely enveloped testis and epididymis.

The reflection of the tunica vaginalis to the testis in the cases of high investment of the cord occurs only at the highest point of the vaginal sac. This is clearly noted in the gross specimen and is also demonstrated in the serial microscopic sections of the entire scrotum.

A study of the literature of these cases convinces me that high investment of the testis and adnexa was present in every reported case. Various expressions are used by different authors to describe this high investment: Twist above the epididymis (Birdsall), intravaginal twist (Edington), the tunica vaginalis extends high upon the cord (Campbell), floating testicle (Lauenstein), like the heart in the pericardium (Lahayville), dangling testicle (Rigby and Howard), intratunical pedicle (Scudder), the cord inserts like a stalk of an apple (Taylor), and dangling in a hazardous and unsupported manner (Meltzer).

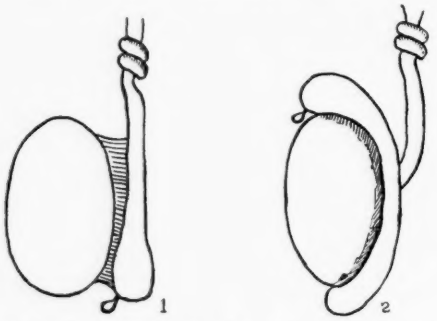

Fig. 4. Illustrating torsion of the spermatic cord in both rotated and unrotated cases.

The presence of other abnormalities observed in torsion cases has frequently overshadowed the most important part of the pathology of torsion, the high investment of the testis and adnexa. The anatomical abnormalities encountered are well summarized by Meltzer. He collected about 9 variations from the normal as reported in the world literature: (1) a very roomy tunica vaginalis; (2) an open tunica vaginalis; (3) absence of the gubernaculum testis and posterior mesorchium; (4) absence of scrotal ligament; (5) abnormal attachment of the common mesentery and vessels to the lower pole of the testis and to the globus minor of the epididymis, so that the testis is attached by a narrow stalk instead of a broad band; (6) elongation of the globus minor; (7) excessive length and poorly attached intravaginal spermatic cord; (8) loose and mobile connections between the testis and epididymis; and (9) loose connections between the scrotal contents and the tunica.

These abnormalities are frequently encountered, being more or less pronounced in a given case. They are not of such a character as to affect the organs proper, the difference being as to the relative topography of the organs concerned, causing a lengthening or shortening of their connecting links. A long

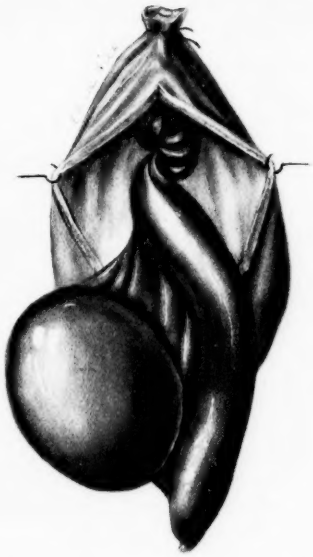

Fig. 5. Specimen removed at operation in Case 2, showing torsion of the spermatic cord in an unrotated testicle with high investment, the testis and adnexa hanging freely in the vaginal cavity.

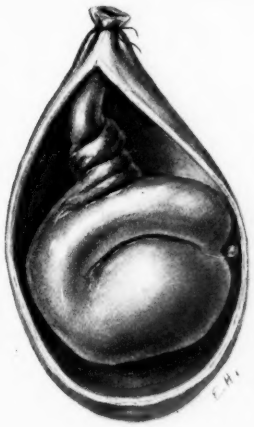

Fig. 6. Specimen removed at operation in Case 1, showing torsion of the spermatic cord in a normally rotated testicle with high investment, both testis and epididymis hanging freely in the vaginal cavity.

mesorchium keeps the testis at a distance from the epididymis. The high investment of these organs and complete envelopment by the tunica vaginalis causes the epididymis to be freely movable and lacking of any attachment posteriorly. The absence of the gubernaculum has never been proved (Campbell); it probably will always be found when looked for. It often appears as a string of tissue on the lateral posterior side of the vaginal sac. The early high investment of the testis and adnexa causing what to all intents and purposes is an actual disuse atrophy of their abandoned guide.

These deviations from the normal syntropy of the testis and epididymis can easily be explained as the result of the early high investment of the testis, adnexa, and cord. Normally during descent the testis and epididymis rotate together on their axes, turning the lower pole of the testis outward and upward, completing a rotation of 180 degrees; the lower pole becomes the permanent upper and the upper pole the permanent lower. The epididymis follows the same 180 degrees turn together with the testis, the lower end of it becoming the upper end or the globus major; while the upper end becomes the permanent tail or globus minor of the epididymis.

Any interference with this physiological rotation, as in early high investment of these organs, must produce situations in which the relative position of these organs will be found in any stage of rotation. The epididymis will either have only one pole, as in our case, or can be found to have completed the turn, or remained in any position midway between these two. The high investment of these organs fixes them in the position found at the time this investment occurred and keeps them there permanently.

It would seem reasonable in view of what has been said, to assume that torsion of the testis and adnexa depends on the freedom of these organs to twist. This freedom is accomplished by the high tunical investment. Instead of being a partially intravaginal body, the testis and adnexa become completely invested by the tunica vaginalis long before the descent is completed. The final stage of the descent is made as a body within a sac. The organs invaginated early will not complete the physiological rotation of testis and epi-

Fig. 7. The cremaster muscle in normal, the muscle bundles extending down upon the spermatic cord, covering the outer part of the vaginal cavity.

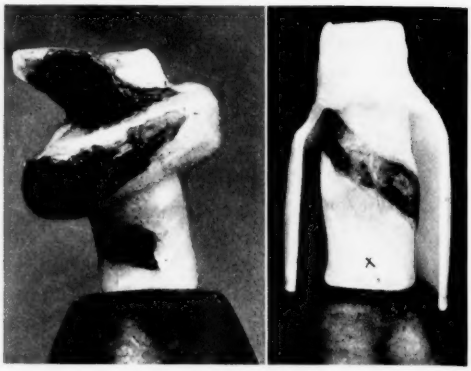

Fig. 8, left. Reconstruction model of the twisted spermatic cord with the cremaster muscle as found in serial sections.

Fig. 9. Model of the spermatic cord in case of torsion after untwisting, showing the spiral band of the cremaster muscle, surrounding the cord inside the vaginal cavity.

didymis remaining permanently in the position they were in before investment was completed.

High investment of the testis and adnexa, however, explains only one part of the problem of testicular torsion; it explains the situation which makes the rotation possible. The other problem concerns the force that actually causes the rotation and holds the structures in the abnormal position with such tenacity as often to make untwisting difficult.

It is generally believed that this force is caused by a strongly contracting cremaster muscle since this is the only contractile motive force in this region. O'Connor has observed "three prominent strands of cremaster muscle reflected low down upon the cord, their origin being just above the site of the torsion."

The cremaster muscle being an extension of the lower end of the internal oblique and transversalis muscles, sends fibers along the spermatic cord in the form of loops extending over the outer part of the vaginal sac (Fig. 3). A contraction of this muscle will pull the spermatic cord and, with it, the testis and adnexa upward, making tension on the vaginal sac. Spasm of this muscle will pull the structures into the groin, 2 cases having been described by Curling, the spasm lasting several days.

In order to determine the part played by this muscle in the case of torsion which we studied reconstructions of it were made from the serial sections. The tissues well preserved were treated with Zenker's solution and embedded in paraffin. Serial sections were made and every fifth one was mounted. These sections were stained with the special Mallory muscle and connective tissue stain, the connective tissues being stained blue and the musculature red. Each section so mounted was then placed under a drawing microscope and the outline of the tissues and muscle bundles was noted on paper sheets. These drawings were later transferred to glass plates, the muscle being painted red and the tissues blue. The glass plates were then placed one on top of the other completely reconstructing the spermatic cord with the twist, the musculature present appearing red through the glass block.

The topography of the cremaster musculature was then transferred onto a rubber cord, the cord having been twisted the same as the spermatic cord. On untwisting this rubber cord the cremaster appeared in the form of a broad band surrounding the cord like a spiral

(Fig. 5). Two wax models were made, one showing this muscle on a twisted cord and the other on an untwisted cord (Figs. 4 and 5).

The relative topography of the cremaster muscle in this case of torsion appears very significant in that it apparently holds the key to the second etiological factor in torsion of the testis. Although the cremaster topography appears the same as in the normal, its relative topography due to the high investment of the spermatic cord is changed. Instead of extending over the outer part of the vaginal sac, as in the normal, in cases of torsion, because of the high investment, the cremaster fibers are carried down into the inner part of the vaginal sac to the lowermost point of the spermatic cord. On sections the muscle can be traced all the way down to the testis (Fig. 6).

In a case of torsion the cord, testis and epididymis form a single movable body in a roomy vaginal sac. The cremaster muscle cannot pull one part of this movable body without affecting the other. A strong contraction of this muscle will rotate the freely movable testis and adnexa. Since the reconstruction models from the serial sections showed that the cremaster muscle was in a contracted state it is indicated that this was the motive force which caused the torsion.

The major factor in torsion of the testis is the high investment of the testis, epididymis, and cord—this permits the cremaster muscle to be carried into the vaginal sac. It is evident that such a freely movable testis with a spiral muscle attached to its stalk will easily become twisted when cremaster spasm occurs.

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OBSERVATIONS ON THE RESPONSE OF THE SAME CHIMPANZEE TO DIAL, AMYTAL, AND NEMBUTAL, USED AS SURGICAL ANÆSTHETICS

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IN human beings one cannot well compare in the same individual the effects of closely related anæsthetics, and it has therefore seemed worth while to report a series of such observations on a chimpanzee. In studying the problem of surgical anæsthesia in primates, we have recently had occasion to administer the barbituric acid derivatives, dial, amytal, and nembutal, to a large chimpanzee for three successive major surgical operations separated from one another by intervals of 1 to 2 months. We look upon the reactions of this animal as particularly significant since the chimpanzee in its neurological behavior (2) and in its response to drugs approaches the human being more closely than other primates such as the baboon or monkey.

The subject of the study was a white-faced, male chimpanzee, aged 4 to 5 years, corresponding with the variety designated by Elliot (1) Pan leucoprymnus. It had been under observation for 3 months prior to its first operation and was in excellent health throughout that period. Full details concerning the three operations are given in our monograph on the Babinski response (2). As far as we are aware, this was the first chimpanzee upon which a surgical operation had been performed under an anæsthetic of the barbituric acid group. We might say, parenthetically, that these drugs offer an almost ideal anæsthetic for neurological work on primates, for in a series of nearly 200 operations on monkeys, baboons, and chimpanzees, we have had only three fatalities (two monkeys and a baboon) attributable to the narcotic. In two instances the dose had been considerably increased owing to the failure of the calculated dose to "take hold" with the accustomed promptness. The special advantages of individual barbituric acid anæsthetics will be discussed below.

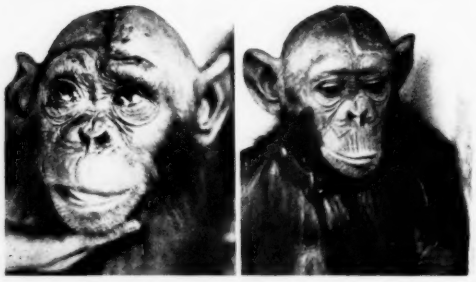

Fig. 1A. Twenty-four hours after first operation; the animal is still under dial, dazed and disoriented.
Fig. 1B. Ten days later, showing healing of the wound.

DI-ALLYL-BARBITURIC ACID (DIAL CIBA)

The advantages of dial as a general anæsthetic for neurological operations on animals (dogs, cats, and monkeys) have been described at length by Fulton, Liddell and Rioch (4). We are able to confirm their findings and have now extended them to include chimpanzees. We have made one further significant observation, namely that in very dry atmospheres animals take considerably longer to recover than in moist atmospheres, owing presumably to the increased loss of fluid through the lungs and skin; thus, in the Thames valley in England monkeys generally recover from dial in 16 to 20 hours, whereas animals of the same species with the same dose made up in exactly the same way require 24 to 30 hours when the drug is administered in the excessively dry, central-heated laboratories at New Haven. With cats the difference is even greater and if no fluid is given, they may require 3 to 4 days to recover fully from a calculated dose. Further observations on the influence of humidity are in progress.

We propose now to describe the reaction of our chimpanzee to dial. The observations have been confirmed in a second animal of about the same age and species, but as the rate of induction and recovery was nearly identical

in the two animals, only the protocol of the first animal will be given.

Preliminary emotional disturbance. The animal had been brought upstairs to the operating room in a cage, a maneuver to which we had accustomed him by carrying it out on the 3 days prior to operation; however, when he saw the syringe being prepared and four or five people standing about, he became aware at once that something was wrong and flew into a tantrum, screaming, kicking, and exhibiting the characteristic facies of a crying chimpanzee—at first his lips were extended as though about to suck, then the lips were drawn back with the mouth open, teeth showing, and he shrieked at the top of his lungs; this alternation of grimaces continued for 4 or 5 minutes during which time there was extensive involuntary defæcation. At 9:04 the animal shrieked two or three times and then vomited, at first unproductively, and eventually he brought up a considerable quantity of yellow fluid which he caught in his hand and promptly re-swallowed.

Injection, December 3, 1930, 9:07 a.m. The animal was caught by five men and held while 5 cubic centimeters of dial (Ciba) was injected intraperitoneally into the left side of the abdomen. As his weight was 12,650 grams this amounted to a dose of approximately 0.365 cubic centimeter per kilogram (10 per cent solution).

Induction. The protocol giving the details of the gradual induction is as follows:

9:07. Injection; no obvious effect after 3 minutes; no screaming or hyper-excitability.

9:10. Put its arm out to be scratched.

9:13. Still alert and looking around to satisfy his curiosity on hearing any sound.

9:14. Peered out of the edge of the cage to observe who was coming in the door.

9:15. Perhaps a little unsteady. Leaning against the back of the cage. No excitement.

9:16. Head a little unsteady. Pupils dilated somewhat. Apparently has difficulty in fixing on an object. Grasped one's hand on putting it into the cage.

9:17. Head definitely unsteady and falling toward the front of the cage.

9:18. Cage opened.

9:19. Again looked out at someone coming in the door.

9:20. Started to lie down in the bottom of the cage.

9:21. Got up and walked out of the cage, turned around and ran back again. Definitely unsteady in locomotion.

9:22. Lay down in the bottom of the cage, making himself comfortable with his head on his left elbow.

9:23. Completely stretched out. Respiration increasing in rate.

9:24. Respiration 42. Eyes shut. Moving hand.

9:25. Completely quiet. Respiration deeper.

9:26. Raised his head on hearing a sound and then dropped off again.

9:28. Respiration 33. Much quieter.

9:40. Still quiet and thought sufficiently deeply anæsthetized for shaving of the head. Respiration 30.

9:50. Animal woke up when his head was being shaved and an additional cubic centimeter of dial was given. After this dose the animal gradually became more deeply anæsthetized, and at 10:00 it was possible to begin shaving.

10:10. Withdrawal reflexes were still present, and it was evident that we could not well proceed with an operation at that depth. The animal was weighed a second time.

10:23. An additional cubic centimeter of dial was given, making a total of 7 cubic centimeters, that is, at this morning's weight, 0.55 cubic centimeter per kilogram. After this the anæsthesia gradually became deeper.

10:30. Placed on the table, at which time there was still some shivering and slight movement of the hands and shaking of the neck muscles when iodine was applied to the scalp, but ether was not required at any point, and one gained the impression that during the operation the anæsthesia became progressively somewhat deeper. Toward the end there was slight movement of the shoulders as we were approximating the skin. On three or four occasions during the operation he coughed, apparently from mucus that had collected in his trachea. The anæsthesia on the whole was entirely satisfactory and just the desired depth. Blood pressure appeared to remain fairly high throughout as there was active oozing on all surfaces during closure.

It will be seen that during the first 10 to 12 minutes after the injection of dial, it had exerted no obvious effect except that the animal became quiet and had no further emotional disturbance. There was no period of excitement at any stage. The respiratory rate remained unchanged and ultimately at the end of 15 minutes the animal gradually fixed himself comfortably in his cage and laid down to sleep, resting his head on his left forearm. His eyes gradually closed, but even at the end of 40 minutes he could still be aroused by vigorous stimulus; after being aroused, however, he dropped off again quickly in apparently normal sleep. At the end of 50 minutes the anæsthetic had exerted nearly its full effect and was supplemented in order to abolish all spontaneous movement.

The reflexes under anæsthesia were of some interest. The knee jerk and withdrawal reflexes became gradually abolished, but reflex coughing persisted throughout as did also the corneal reflexes. Shivering was in abeyance and at the end of the operation (8 hours after

the injection) the rectal temperature had fallen to 36 degrees C. The surgical procedure consisted of left sided bone flap with identification of the motor area by faradic stimulation and extirpation of the foot area with the Bovie electrical cutting knife.

Recovery. The stages of recovery from the anæsthesia will be indicated in hours.

1st to 2nd hours. Induction.

2nd to 8th hours. Operation.

9th hour. Respiration 38 per minute. Animal deep. Temperature 38.1 degrees C.

13th hour. Respiration 36. Animal could not be aroused even by vigorous stimulation.

24th hour. Rectal temperature 37.6 degrees C. Respiration 25. Grasping movements, but the animal was still deeply anæsthetized. Occasional spontaneous movement of the left arm and leg. Pupils dilated; marked conjugate deviation of eyes to the right side.

30th hour. More spontaneous movements, but eyes are still deviated (see illustration) and the animal can be aroused only with difficulty. Primitive Babinski reflex present in the right hind foot. Knee jerk absent.

34th hour. More spontaneous movement, but the animal is still dazed, and not yet sitting up. Eyes moving more freely than during the thirtieth hour.

48th hour. When first observed the animal was sleeping profoundly, but when aroused it opened its eyes, looked around in rather dazed fashion and then drank a large quantity of fluid, the first taken since its operation. Reflexes more brisk, but whenever the animal was left to itself it dropped off again to sleep.

55th hour. Definitely brighter, but still somewhat dazed and objected to being disturbed.

61st hour. Sleeping deeply. When aroused, he sat up in his cage and seemed fairly well recovered, but somewhat slow of movement.

72nd hour. He had quite thrown off all effects of dial; alert, active and obstreperous. Following this the animal has made entirely satisfactory postoperative recovery.

From the preceding protocol it will be evident that the chimpanzee requires nearly 3 full days to throw off the effects of a surgical dose of dial. No fluid was taken spontaneously during the first 24 hours; during the second day the animal was dazed and sleepy, but it took food and fluid. In the second chimpanzee of the same age and weight which was subjected to the same operation, the recovery required the same length of time. In both instances, it was considerably longer than the period of postoperative recovery of monkeys from the same drug.

SODIUM AMYTAL

Sodium amytal has been used extensively in cats and dogs, and in man (5) but we have found no record of its use in the lower primates apart from the brief report of F. D. Weidman recently issued by the Philadelphia Zoological Society (8), and it has not been used previously on a chimpanzee. The same animal was used as in the previous operation. In the 7 weeks' interval he had fully recovered his strength and had increased in weight. Assuming that the dose required would be similar to that necessary for monkeys, 6 cubic centimeters of a freshly made solution of 10 per cent sodium amytal was given intraperitoneally, making a dose of 44 milligrams per kilogram (the animal's weight having increased to 13,550 grams since the last operation). When satisfactory anæsthesia had been secured, a right sided bone flap was turned and the right foot area was extirpated after its margins had been defined by faradic stimulation. All stages of the procedure were similar to those carried out for the first operation (extirpation of the left foot area, see 2).

Induction, January 21, 1931, 8:23 a.m. Just before the injection the animal had an emotional upset similar to that described above. He was held as before and no difficulties were encountered during the intraperitoneal injection. The detail of the induction are as follows:

8:23. Injection. No obvious effect during the first minute.

8:24. Placed back in its cage; stopped shrieking and was quiet.

8:25. Still no obvious effect, apart from looking somewhat subdued.

8:26. Much quieter. Stopped moving. Eyes still open.

8:26. Put his head down in the bottom of the cage.

8:27. Up, but swaying and again put his head toward the bottom of the cage.

8:28. Obvious ataxia in the movements of his hand. Resting his head against the corner of the cage; looking sleepy.

8:29. Arranging himself comfortably for sleep by putting his head on his right elbow. Eyes closing. Induction now proceeding very rapidly.

8:30. Well "under," but responding very feebly to strong pinching.

8:31. *Babinski response.* Rather to our astonishment when the right sole was squeezed the toes moved upward very little, but the hamstring muscles and all the flexors of the extremity contracted vigorously as on the day following operation. A

very gentle pinch of the sole caused a vigorous hamstring jerk. It would seem that this reaction had been held in abeyance while the animal was awake and emerged as a primitive form of response while narcotized. The left hind limb showed no response whatsoever either of toes or hamstring muscles; it was relaxed and motionless.

8:32 to 8:35. Reactions of the right and left toes still unchanged, animal scarcely responding at all. Respiration regular. Some shivering. Pulse strong.

9:03. On the table ready for operation but occasionally moving his hand and responding by turning his head when his ear is pinched. 1 cubic centimeter sodium amytal given, making a total dose of 7 cubic centimeters, i.e., 52 milligrams per kilogram.

9:15. 1 cubic centimeter sodium amytal given.

9:30. Animal still rather too light and an additional cubic centimeter of sodium amytal was given. After this he quieted down and the anæsthesia became fairly deep. His respiration throughout the operation remained regular, somewhat more shallow than normal, and increased in rate toward the end. There was no movement, except during the stimulation of the cortex, and no vocalization; no respiratory difficulty. The heat center had evidently been disturbed for there was no shivering during the operation and the body temperature gradually diminished, being 36.1 degrees at the end (3:00 p.m.).

With an initial dose of 44 milligrams per kilogram of body weight, between 7 and 8 minutes elapsed before the animal was "down," but it had begun to show obvious effects of the drug 3 to 4 minutes after the injection. When dial was used the animal had appeared quite unaffected even at the end of 12 minutes, and it was more than 20 minutes before it was "down."

The dose of amytal had to be supplemented ultimately to 65 milligrams per kilogram. This proved entirely adequate for the whole procedure, and as with dial, it caused no appreciable depression of excitability of the motor cortex. With neither drug was there a period of excitement during induction, and in the early stages the animal in each case went through all of the rather striking preliminaries of arranging itself for sleep. In the second chimpanzee which received sodium amytal induction lasted also 6 to 7 minutes and the ultimate dose (greater than was necessary) was 70 milligrams per kilogram.

The speed of recovery from sodium amytal stands in about the same relation to dial as the speed of induction, as is evident from the following protocol:

Recovery. The stages of recovery from the sodium amytal after the second operation are indicated as follows in hours:

1st hour. Induction.

3rd to 7th hour. Operation.

8th hour. Deep, breathing regularly; all reflexes abolished; continuous temperature readings obtained from the rectum.

9th hour. X-rayed; slight spontaneous movements of hands and at 5:10 p.m. definite vocalization; temperature only 96.8 degrees.

11th hour. Temperature 99 degrees.

12th hour. Temperature 100 degrees; spontaneously raising his head (8:10 p.m.), opening his eyes and moved his arm; but quickly dropped off again; reflexes had returned in right lower extremity.

13th hour. Temperature 101 degrees; on supporting his head (9:30 p.m.) he was able to drink 300 cubic centimeters of milk and then dropped off to sleep. Reflexes more vigorous than at 8:00 p.m.

24th hour. Temperature normal; sitting up, moving about fairly actively, but looking a little subdued; taking food and fluid freely.

31st hour. Much more alert; movement quicker; animal obstreperous and protesting. All effects of anæsthetic were now quite worn off. Feeding freely; eating a large apple without evidence of discomfort in temporal muscle.

The recovery from sodium amytal thus followed a course similar to that seen in human beings subjected to this anæsthetic; i.e., the chimpanzee was able to drink at the end of 13 hours and was sitting up after 24 hours. At the end of 30 hours, all effects of the anæsthetic had disappeared. There was no stage of excitement during recovery and nothing to suggest despondency or mental depression after the immediate effects of the anæsthetic had worn off. Respiration was materially depressed, and the heart was not embarrassed.

NEMBUTAL

Nembutal (sodium ethyl-1-methyl butylbarbiturate), one of the new barbituric acid derivatives, prepared by the Abbott Laboratories of Chicago, has recently been used by Lundy (6) and others (5, 7) in human beings. We had employed the drug in this laboratory for several months for operations on dogs, cats, and monkeys prior to its being used for the chimpanzee; it proved particularly satisfactory for brief procedures in which recovery was desired the day of operation. In several instances after a nembutal injection which had given profound narcosis, monkeys were sitting

up drinking water within 4 to 5 hours. We observed that nembutal differed from dial and amytal in that it produced a fairly marked depression of the excitability of the motor area in anæsthetic doses (3), and it is therefore not suited for investigations requiring faradic stimulation of the cortex. We have since observed that it occasionally causes very marked excitement, both in dogs and in monkeys, during the early stages of induction. We are inclined to attribute this to depression of the cortex prior to its affecting the hypothalamic centers.

As our chimpanzee seemed quite recovered from its second operation at the end of 3 weeks, and as we wished to give a demonstration of Horner's syndrome to the classes in physiology, the left cervical sympathetic chain was removed under nembutal anæsthesia. The details of the administration of the drug are as follows:

Induction, February 12, 1931, 11:48 a.m. The animal was held in the usual way and a dose of 30 milligrams per kilogram of nembutal in aqueous solution was injected intraperitoneally. The dose used was slightly less than that found previously to have been adequate for monkeys.

11:48. Injection. No effects were seen during the first 2 minutes.

11:50. Animal in its cage looking about, still apparently unaffected.

11:51. First signs of unsteadiness; settled down in the bottom of his cage, lying on his left side in a comfortable position.

11:52. Still rearranging himself, turning now onto his back; later he turned onto his abdomen.

11:53. Marked ataxia in all movements.

11:54. Completely relaxed, in fairly deep surgical anæsthesia. On lifting him to the examining table, the Babinski response was seen to have reverted to its primitive condition associated with marked triple flexion; the ears were still cool.

11:58. Deeper; stimulation of plantar surfaces gave abrupt withdrawal with no movements of the toes.

12 noon. Still deep; blood drawn from femoral artery.

1:00. Profoundly narcotized, not responding.

2:00. The animal continued fairly deep until 2 p.m., when its neck was shaved prior to operation. It was evident that he had begun already to recover from the anæsthetic and that a second dose would be necessary.

2:30. Second injection, 3 cubic centimeters 5 per cent nembutal, making a total dose of 40.5 milligrams per kilogram. After this, the anæsthesia was sufficiently deep for the operation. The left cervical sympathetic chain was removed along an inch of its course.

In this instance the induction with nembutal ran a course very similar to that with sodium amytal, being slightly more rapid, particularly between the fifth and sixth minutes; at the end of the sixth minute the animal was in deep surgical anæsthesia, whereas this degree of anæsthesia did not appear until about the eighth or ninth minute after a similar dose of sodium amytal. The respiration was somewhat more depressed and shallow, but there was no difference evident in the general effects of nembutal on the circulation. In dogs, cats, and monkeys, we have observed rather a marked vasodilatation of the cutaneous vessels 7 or 8 minutes after injection of nembutal, but this gradually passes off. The very great speed of induction and the effect on respiration appear to be the only alarming features of the anæsthesia. We have used the drug repeatedly in doses up to 45 milligrams per kilogram with only one fatality (a mature baboon which had sudden cessation of respiration 3 hours after the drug was given), but we feel that a valuable animal under nembutal should never be left without nursing care until it begins to show signs of recovery.

Our observations on recovery from nembutal are less complete than in the case of the other two anæsthetics. Most animals, e.g., monkeys and baboons, appear to recover within about half the time required after sodium amytal.

Recovery. The details of the recovery of the chimpanzee from his third operation (under nembutal) are as follows:

1st hour. Induction.

2nd hour. Deep; respiration shallow; reflexes greatly depressed.

3rd hour, i.e., 2:20 p.m. Animal recovering rapidly and second dose of nembutal necessary (making a total of 40.5 milligrams per kilogram).

3rd to 5th hour. Operation.

6th hour. Still sleeping profoundly, but movements of the hand could be obtained on vigorous stimulation.

8th hour. Reported still asleep, but unfortunately the animal was not stimulated.

20th hour. Fully recovered from its anæsthetic, alert, active, with no sign of mental depression or languor; taking fluid freely. The animal exhibited a marked left sided Horner's syndrome immediately

after operation, but the difference in size of the pupils was very much more evident after recovery from the anæsthetic.

Though monkeys have occasionally shown periods of excitement when subjected to nembutal, we did not encounter it in this or the other chimpanzee to which the drug was given, and we did not observe a period of excitement during recovery. Another chimpanzee which received nembutal drank water after 6 hours and was up and about at the end of 10. The observations are in harmony, therefore, and indicate that the rate of recovery from nembutal is nearly twice as rapid as from sodium amytal.

DEDUCTIONS

Since the preceding observations were all made upon the same chimpanzee, and since we secured approximately the same depth of anæsthesia with each drug studied, we believe that the results allow us to make an accurate comparison of the properties and virtues of the anæsthetics used.

Dial can be recommended for any operation on monkeys or higher apes in which it is desired to keep the animal quiet for several days after the operation. For 24 hours it is likely to remain deeply narcotized, after which it is usually dazed for a further 18 to 20 hours, during which time, however, it will take fluids freely by mouth without evidence of fear or protest. This is particularly advantageous in ferocious animals, which with other anæsthetics are likely to make sudden movements dangerous to their wounds and to the examiner. In view of the very long postoperative stupor, we are not of the opinion that dial would be satisfactory as a surgical anæsthetic for human beings, but we are convinced that it could be used with complete safety, and perhaps to advantage, in certain cases of maniacal excitement. The liquid preparation of dial (Ciba) can be used in chimpanzees in doses up to 0.55 cubic centimeters per kilogram of body weight, being thus somewhat greater than the dose required for monkeys (0.45 cubic centimeter).

Though we have lost a chimpanzee as a result of a pulmonary embolus following amytal anæsthesia, we believe that this accident was fortuitous and that sodium amytal is a safe anæsthetic for chimpanzees and other primates. It is to be recommended if one desires to have the animal up and about within 24 hours. The dose for a chimpanzee appears to lie between 50 and 70 milligrams per kilogram, a dose of 65 milligrams intraperitoneally having been followed in the present animal by recovery in 14 hours.

Nembutal is an almost ideal anæsthetic, administered intraperitoneally, in all cases in which the operation is not to last longer than 2 hours and in which rapid recovery is desired. Induction is generally complete in 5 to 6 minutes and recovery usually occurs in as many hours, using a dose of 35 to 40 milligrams per kilogram of body weight.

SUMMARY

The barbituric acid derivatives, known under the trade names, dial, amytal, and nembutal, have been used extensively as surgical anæsthetics for neurological operations (monkeys, baboons, and chimpanzees); their properties have been contrasted and exemplified by a careful analysis of the responses of the same chimpanzee to each of the three drugs used as anæsthetics for three major neurological operations, separated from one another by periods of 1 to 2 months. The results of this study may be summarized as follows:

	Dose (per kg.)	Induction (minutes)	Recovery (hours) Swallowing	Up
Dial (Ciba)....	55 mgm.	25	30	48
Sodium amytal.	65 mgm.	8	13	20
Nembutal.....	40 mgm.	5	6	10

The advantages of each of the anæsthetics have been summarized briefly in the discussion. Nembutal, though an ideal anæsthetic for a brief operation, is unlike dial and amytal in that it depresses the excitability of the motor cortex.

Recovery from the barbituric acid anæsthetics takes place more rapidly in a moist than in a dry atmosphere.

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THE SOLUTION OF CHOICE IN PROCTOCLYSIS

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VERY little appears in the literature on the subject of proctoclysis *per se* but a host of material is present on the method of introducing the solution chosen. In view of this fact it has occurred to us that a comprehensive study of the relative merits of the various solutions suggested from time to time, might be of some value. Although Lawson, in 1908, made the first observations along these lines, the subject was apparently dropped until 1912 when Trout published his clinical study on the comparative merits of tap water and physiological sodium chloride proctoclysters (10). Working on 400 postoperative cases, regardless of the type of operation they had undergone, and using the Murphy drip technique, Trout noted that ordinary tap water was far better absorbed from the colon than the physiological saline. The actual results indicated that approximately 400 cubic centimeters more of tap water were absorbed per 24 hours than of the 0.9 per cent sodium chloride. He further suggests that if the recommendation of Murphy would be followed (that of pushing the clysis to 18 pints a day) the patient would absorb nearly 81 grams of the salt per diem. The latter figure is something over the normal intake for a month.

In order to ascertain the current ideas regarding the subject, two hundred questionnaires were sent out to larger hospitals of the country with the request that they be filled in. The questionnaires contained lists of some twenty solutions suggested as clysters, and the staffs of the hospitals were asked to check the solutions in the order of their preference. Seventy-eight answers were received and the tabulation indicated an overwhelming preference in favor of three solutions; tap water, 0.9 per cent sodium chloride, and 5 per cent glucose. Tap water was listed as third choice, preference being about equal in regard to the two other favored solutions. During a recent tour of the European clinics, it was noted that the same solutions were generally used if, indeed, the practice of proctoclysis was not discontinued completely in favor of hypodermoclysis or intravenous infusion. From the returned questionnaires and from personal contacts, we could not fail to have it impressed upon us that the reasons for using this or that solution were often extremely vague and many of them without even clinical foundation.

At the present time a great deal of discussion centers about the subject of glucose absorption from the bowel or, more properly, the colon. Bremer, in 1906, making comparisons of fresh and prepared specimens of the small intestine and of the colon, watched the absorption of proteins and fats but says that no carbohydrates can be absorbed. He suggests protein nutrients. Nagel, in 1909, states that glucose has been shown by Czerny and Latschenberger to be absorbed in patients in whom the large intestine or part of it had been completely cut off from the small intestine. He says the same results were obtained by Heile in dogs especially operated upon for this purpose. Nagel also calls attention to the

work of Schonborn, who alleged that a glycosurea could be produced by injection of glucose per rectum. Reach, in 1902, had investigated the change in respiratory quotient after rectal injections of glucose and had come to the conclusion that it was absorbed, although slowly. Hari and Halasz, in 1918, showed a rise in respiratory quotient after rectal injections of glucose in dogs in whom the small gut had been completely ligated off from the large bowel, and state further that an actual glycosurea may be produced in this manner. Ornstein, in 1918, adopted the washing out method, in his investigations on rectal feedings on dogs, and showed that at least *some* absorption takes place and asserts that if glucose be given with starch, a complete absorption will take place. Tallerman, in 1919–20, working on 8 patients, concludes that glucose is absorbed by the colon although much slower than by mouth. Levi noted that a small rise of the blood sugar took place in 11 of 16 patients that received glucose retentions. McNealy and Willems, in 1929, noted that very little if any absorption took place from the colon in dogs.

In the present work, 21 solutions were finally chosen to compare for the work which was to be done on the dog and the human. We did not accept all of the solutions suggested in the questionnaires because we believed that the concentrations which we used were representative and that conclusions as regards those offered could be drawn from our work.

The following solutions were used:

½ Per cent sodium bicarbonate.
1 Per cent sodium bicarbonate.
2 Per cent sodium bicarbonate.
½ Per cent sodium bicarbonate in 1 per cent glucose.
½ Per cent sodium bicarbonate in 5 per cent glucose.
2 Per cent sodium bicarbonate in 5 per cent glucose.
½ Per cent glucose.
1 Per cent glucose.
5 Per cent glucose.
25 Per cent glucose.
½ Per cent calcium chloride.
0.7 Per cent sodium chloride.
0.9 Per cent sodium chloride.
Dextrin solution.
  Dextrin, 100gm.
  Sodium chloride, 2½gm.
  Alcohol, 5c.cm.
  Water, 300c.cm.
Tap water.
Distilled water.
Locke's solution.
Ringer's solution.
Commercial water solution.
  Disodium phosphate, 0.03gm.
  Potassium chloride, 0.01gm.
  Sodium chloride, 0.06gm.
  Sodium bicarbonate, 0.57gm.
  Calcium bicarbonate, 0.07gm.
  Mag. bicarbonate, 0.01gm.
  Water to 100.0c.cm.
10 Per cent dextrin in 0.9 per cent sodium chloride.
Peptone solution.
  Witte peptone, 60gm.
  Sodium chloride, 2½gm.
  Alcohol, 9c.cm.
  Water, 300c.cm.

EXPERIMENTAL WORK ON DOGS

Acute conditions. The animals for experiments in acute conditions were invariably given enemas of warm tap water about 1 hour previous to the experiment in order to empty the bowel. We realize that here we may have introduced an element of error but since all dogs were treated alike the latter is perhaps equalized. The enema was given rather than waiting until the animal was narcotized to clean the fæces out of the bowel because it was realized that the removal of the hard excreta would traumatize the bowel. Sodium barbital anæsthesia by the intramuscular route was chosen because of the small amount of water necessary to dissolve it, thus making it preferable to the oral route and the greater required volume of water. The peritoneal route was discarded because it was noted that a considerable amount of peritoneal effusion takes place subsequent to the injection. Intravenous infusion on several occasions rendered the animals useless by shock, hence was not used.

We chose sodium barbital (in doses of from 200 to 275 milligrams per kilogram) for our work rather than ether because of the necessarily long period of experimentation—some 6 hours. The drug seemed to be ideal for the purpose. In about 95 per cent of the experiments the animal retained active reflexes throughout, including that of the cornea. The animals generally gave some indication of sensibility when the solutions were changed, in that traction on the colon was followed by cessation of respiration. In some instances it was necessary to reinforce the anæsthesia with ether while the solutions were being changed. It was interesting to observe, however, that

even though our animal was in a condition approximating shock (with cold intestines, slow heart, and respiration) the results were of the same general order.

A midline incision was used, extending from the umbilicus to the pubes. The colon was then picked up and a glass cannula introduced in close proximity to the ileocæcal valve. This was secured by a pursestring suture. A similar cannula, secured by pursestring sutures was then introduced into the rectum. The small bowel was tied off at its junction with the colon. The large intestine was then flushed out with warm tap water and gently stripped, and the first solution was introduced.

We realized that, since we were dealing with the relative merits of various solutions, the first criterion in the case of the salt solutions at least, was the relative rate of absorption in regard to their fluid content. To this end we decided to run our solutions in groups of five and these were alternated in their sequence from day to day. Thus a solution which was run first one day would be run last the next day and the others would advance toward the top of the list. After five experiments, when each solution had been run first at least once, the order was completely reversed and another five experiments performed in the new order. We could in this manner be sure that the relative rate of water absorption or solute disappearance noted was the true criterion and was not the result of one solution sensitizing the gut toward that solution next in order. We were also interested in seeing that, in our experiments with glucose, as much error as possible arising from the carbohydrate remaining in the bowel after washing could be eliminated.

The time interval chosen was 45 minutes for each on a given solution. We believed that in such a period any changes likely to take place could be readily demonstrated. At the end of this period the bowel was gently stripped and further exhausted of its fluid content by air pressure. The latter method of emptying the bowel, used in conjunction with the apparatus to be described, makes the procedure quantitative. The bowel was washed between each two solutions with warm distilled water.

We have always been accustomed to some method of stripping the gut because we have noted that unless this is done more or less of the fluid remains to confound the results. It was also our practice in our acute experiments to wash the bowel with distilled water in amounts equal to the original solution used in order to remove the last vestige of the salt introduced. These washings were then combined with the solution taken from the gut and the total concentration worked out from the latter.

The apparatus used consisted of a pressure bottle in which was also kept the solution (Fig. 1). Air pressure from the line was brought to the bottle and maintained at a constant pressure by a mercury pressure flask. Thus the manometer in the pressure bottle was maintained at a given pressure by fixing the end of the air outlet the required distance below the surface of the mercury to keep such a pressure. Hence any change in the line pressure above that set in the bottle would cause more air to flow out through the mercury. In addition to this, if the pressure within the bowel became greater than that within the stock bottle, the fluid in the bowel would flow back into the latter. A drop in the pressure in the bowel due to absorption or tonus change necessarily caused more fluid to go into the bowel.

The fluids were always introduced into the bowel at 37.5 degrees C. No attempt was made to keep the stock fluid at a constant temperature because the amount going into the bowel at any one time was very small (usually at the rate of less than 1 cubic centimeter a minute into a total volume of around 100 to 150 cubic centimeters). In the case of a rapid tonus change within the bowel the amount of cold fluid introduced into the bowel was minimized by the fact that the time interval chosen did not allow the temperature ever to fall as low as the room temperature.

Our reasons for using this apparatus were many. Our chief concern was in the regulation of the pressure factor. We early recognized that on the basis of Hamburger's work, our pressure value had to be constant if we were to determine true values. In addition to this we wished to have an excess of fluid over that introduced into the bowel so that we might assume that all of the mucosa reached by the

original introduction of fluid would be maintained at a constant rate of absorption throughout.

The pressure used was 9 centimeters of water pressure as registered on our manometer. It was found later, in the work on dogs with chronic conditions, that this was just sufficient to overcome the intra-abdominal pressure and allow the fluid to flow in without provoking an emptying movement of the bowel.

During this and subsequent work, we have demonstrated many practical uses for the apparatus other than its special use in intestinal absorption experiments. The mechanism lends itself very readily to intravenous infusion of fluids as well as hypodermoclysis. By regulation of the output one may infuse over a period of hours with excellent results. In the infusion of blood, the samples must be citrated or defibrinated but no other precaution is necessary. Attention must be paid, however, to the level of the fluid in the bottle, so that air is not introduced into the circulation.

As earlier suggested, the 21 solutions used were arbitrarily divided up into groups of 5 with no attempt to segregate the salt solutions from the glucose solutions. It was felt that in this manner we could make a more complete study.

The first group consisted of 5 per cent sodium bicarbonate, tap water, Ringer's solution, 1 per cent sodium bicarbonate and 0.9 per cent sodium chloride. The second group consisted of 1 per cent glucose, 0.5 per cent calcium chloride, 0.7 per cent sodium chloride, Locke's solution, and 5 per cent glucose. The third group consisted of a commercial alkaline water which was supposedly high in calcium and carbon dioxide, distilled water, 0.5 per cent sodium bicarbonate in 1 per cent glucose, 2 per cent sodium bicarbonate, and 2 per cent sodium bicarbonate in 5 per cent glucose. The fourth group consisted of 5 per cent glucose, 10 per cent dextrin in 0.9 per cent sodium chloride, 0.5 per cent sodium bicarbonate in 5 per cent glucose, dextrin solution and peptone solution. The results on each series will be discussed in detail. Series 5 consisted of those salt solutions which evinced superiority in their respective groups. Series 6 were those glucose solutions chosen for the same reason. In the latter we were concerned with the rôle of the sodium bicarbonate as well and so used one of our poorest absorbed solutions, 5 per cent glucose, for purposes of comparison. The "series 5" experiments were run twice, the second time being a year later. The object was two fold; to determine which of the solutions was best absorbed and secondly, to determine the fate of the solutes. Series 6 was also run one year later than the other experiments but it is interesting to note that the results gained are in total conformity with those of the previous year.

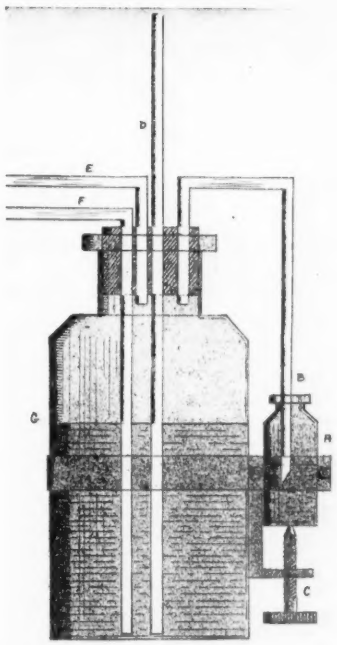

Fig. 1. A drawing of the pressure bottle used in most of the experiments. *A*, the mercury bottle for overflow of air; *B*, air overflow tube; *C*, screw for raising or lowering the mercury bottle; *D*, water manometer; *E*, air intake tube; *F*, outflow tube to the gut; *G*, pressure bottle containing solution.

Unanæsthetized dog experiments. Four dogs were used for the experiments in chronic conditions. The series of experiments were run for the express purpose of checking up on the results which were obtained in the acute conditions with the work done under barbital.

TABLE I.—SERIES 1

Solution used		Experiment No.										Total ave.
		1	2	3	4	5	6	7	8	9	10	
.5 Per cent $NaHCO_3$	c.cm.	67.0	30.0	23.0	27.0	21.0	19.0	30.0	20.0	18.0	23.0	28.7
	pt.	5	5	5	5	5	5	5	5	5	5	5.0
Tap HOH	c.cm.	53.0	16.0	20.0	23.0	14.0	17.0	25.0	10.0	12.0	20.0	21.0
	pt.	3	3	4	3	3	4	4	3	3	4	3.4
Ringer's	c.cm.	47.0	20.0	16.0	25.0	9.0	11.0	15.0	7.0	12.0	16.0	17.8
	pt.	2	4	3	4	2	2	3	2	3	3	2.8
1 Per cent $NaHCO_3$	c.cm.	40.0	1.0	14.0	12.0	16.0	14.0	9.0	6.0	15.0	11.0	13.8
	pt.	1	1	1	2	4	3	1	1	4	2	2.0
.9 Per cent NaCl	c.cm.	57.0	12.0	15.0	4.0	9.0	2.0	11.0	13.0	6.0	3.0	13.2
	pt.	4	2	2	1	2	1	2	4	2	1	1.9

In all charts on acute experiments we have recorded not only the number of cubic centimeters absorbed but have designated the relative rate of absorption by "points." Hence if in one experiment a given solution was best absorbed it received 5 points because it was best of 5 solutions. The next best absorbed received 4 points and so on. The term "c.cm." has reference to the amount absorbed or excreted as the case may be.

Cæcostomies and perineorraphies were made on each of the animals, females being chosen for ease in catheterization. The incisions were made in the midline and the cæca were brought out through stab wounds in the left rectus, the perineal operation being done at the same sitting. After the completion of the latter operation, the cæcum was clamped with a long hæmostat and cut; the free cut edge was then cauterized for hæmostasis and the original incision through the abdominal wall was covered with a small strip of gauze soaked in collodion. The latter rapidly dried and formed an excellent covering for the wound. Operating in this fashion we were able to complete the work in one stage and at the same time to expose the animal to a minimum of infection. Dogs so operated upon may be used in 1 week.

In series 7 and 8 the operations were those performed for chronic conditions and those solutions were used which appeared to be superior in series 5 and 6. In series 7 and 8, due to the fact that we were unable to control as accurately the amount of solution possibly absorbed, it was determined to make the periods that each solution was run, longer. The time chosen was 3 hours or four times the experimental period in the acute conditions. Only 2 solutions were run on each dog each day due to possible fatigue of the animals over such a long period of time. The solutions were so rotated that each was compared with the others at least twice, being run first once and then last the next time.

The experiments for chronic states were run on animals that had cæcostomy openings into the left rectus so that the muscle could be used as a valve. The ileocæcal sphincter helped a great deal in maintaining a water tight system. Most of the error introduced by the leakage of fluids was eliminated by the use of Templeton's apparatus (Fig. 2). This makes use of an ordinary nipple from a nursing bottle which is pierced by the glass tube. When introduced into the bowel the end flares out and, combined with the pressure of the bowel upon it, seals the latter fairly well as far as the escape of fluid is concerned. One of these was also introduced into the anus for drainage purposes. It was noted in the course of the experiments that the same methods used, with the exception of the bowel stripping, in the acute conditions could be used on the animals with chronic conditions. In the latter when emptying the gut and applying air pressure, it was customary to apply pressure on the dog's abdomen to force the fluids out.

In the work done with these animals it was early realized that any analysis of the salt content of the fluids drained from the bowel would be practically worthless because of the error introduced by the fæces retained in the crypts of the bowel. On the basis of our work on the glucose, however, (controls on distilled water)

we decided to continue the analysis of the sugar solutions. The results obtained are outlined.

The described method of observation of absorption from the large bowel was chosen in preference to the closed loop because we felt that in spite of the error possibly introduced by fluid escaping from the small bowel and retained fæces after the enemas, it was far more physiological and nearer to human practice. In the closed loop method we would have to deal with a constant mucus secretion which would have to be washed out, and a constant leakage from the ileostomy opening. This of itself would introduce an error because of the disturbance to the water balance of the animal, since the function of the colon is normally to resorb the water of substances in course of digestion. A criticism may be raised on the basis that the nipple introduced shuts off the opening of the ileum into the colon and hence may conceivably cause a piling up of materials in the small bowel during the course of the experiment and in some reflex fashion alter the results from those which would otherwise be obtained. We do not believe that this is true for our animals were fed about 16 hours before the data were checked, hence the bowel was presumably free at time of experiment.

In our observations on urinary excretion, controls were run on amounts and total acidity before and during the course of the experiments. The control periods were variously from half an hour to an hour, and the excretion was calculated on the basis of 1 hour.

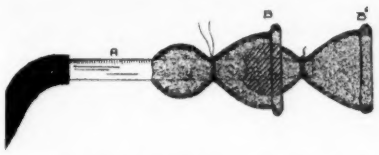

Fig. 2. Templeton's apparatus. *A*, Glass tube; *B* and *B'*, soft rubber nipples tied over tube.

The animals were kept on pads during the course of the experiments and frequently went to sleep. They were covered with towels to keep them warm and to quiet them.

By the simple expedient of providing a smaller gauge intake tube than the outlet, we were able to cause a lag in the solution going back into the bottle after a colon contraction. We then connected a water manometer to the outlet at the anus and obtained by this method a tracing of colonic activity. Thus we had an apparatus for the observation of absorption of a given solution and could determine its effect upon the activity of the bowel itself. The idea presents many possibilities of the observation of the pharmacological properties of various drugs upon the colon. Thus we can use the chosen drug either in the proctoclyster or by substituting tap water, etc.; for the latter we can determine the effect of hypodermically administered solutions.

RESULTS

Acute conditions. As has been previously mentioned, our list of 21 solutions was arbitrarily split up into groups of 5 for comparison

TABLE II.—SERIES 1, URINARY EXCRETION

Solution used		Experiment No.										Total ave.
		1	2	3	4	5	6	7	8	9	10	
.5 Per cent $NaHCO_3$	c.cm.	9.0	0.5	3.0	6.0	8.0	10.0	4.5	14.0	3.0	0.0	5.8
	pt.	5	1	1	4	5	2	1	3	2	2	2.6
Tap HOH	c.cm.	9.0	2.0	4.0	1.0	4.0	6.0	10.0	17.0	7.0	5.0	6.5
	pt.	5	2	2	3	4	1	2	4	3	5	3.1
Ringer's	c.cm.	1.0	3.0	4.0	0.0	2.0	12.0	11.0	18.0	1.0	0.0	3.6
	pt.	1	3	2	2	2	3	3	5	1	2	2.4
1 Per cent $NaHCO_3$	c.cm.	4.0	6.0	10.0	8.0	3.0	16.0	15.0	11.0	9.0	4.0	8.7
	pt.	4	5	5	5	3	5	4	2	5	4	4.2
.9 Per cent NaCl	c.cm.	3.0	5.0	8.0	0.0	1.0	13.0	10.0	2.0	8.0	2.0	6.0
	pt.	3	4	4	1	1	4	5	1	4	3	3.0

TABLE III.—SERIES 2

Solution used		Experiment No.										Total ave.
		1	2	3	4	5	6	7	8	9	10	
1 Per cent glucose	c.cm.	25.0	15.0	30.0	40.0	20.0	16.5	25.0	22.0	25.0	28.0	24.65
	pt.	5	4	3	4	5	4	4	5	4	5	4.3
.5 Per cent $CaCl_2$	c.cm.	18.0	20.0	41.0	21.0	18.0	25.0	18.5	16.0	29.0	24.0	23.05
	pt.	3	5	4	2	4	5	3	4	5	4	3.9
.7 Per cent NaCl	c.cm.	21.0	12.0	45.0	44.0	15.0	12.0	28.0	9.0	20.0	24.0	23.0
	pt.	4	3	5	5	3	3	5	3	3	4	3.8
Locke's	c.cm.	8.0	6.0	10.0	21.0	7.0	4.0	10.0	2.0	4.5	7.0	7.95
	pt.	2	2	2	2	2	2	2	2	2	2	2.0
5 Per cent glucose	c.cm.	−2.0	−4.0	3.0	2.0	−10.0	−14.0	−8.0	−11.0	3.0	5.0	−4.1
	pt.	1	1	1	1	1	1	1	1	1	1	1.0

purposes. The odd one left over, 25 per cent glucose, was run in a separate series (series 7).

Those solutions which showed the best absorption rates in the early series were grouped together in the fifth and sixth series for further elimination. As may be expected, the differences here are not so striking as previously. However, it may be seen that 0.5 per cent calcium chloride was slightly better than the 0.5 per cent sodium bicarbonate and commercial water solutions. This group consisted wholly of the inorganic salts. The sixth group, made up of glucose solutions primarily, was run in an attempt to judge which of these were best suited for absorption purposes. In this series the 1 per cent glucose was best absorbed as far as fluid content was concerned and the 0.5 per cent glucose and 0.5 per cent sodium bicarbonate in 1 per cent glucose were equally well absorbed. The actual amounts of glucose absorbed per cubic centimeter followed the fluid absorption in comparatively close agreement (about 1 gram per 100 cubic centimeters in the case of the 1 per cent glucose).

A short table of comparisons of the different solutions follows:

TABLE OF COMPARISONS

Solutions used:	Average absorbed:
0.5 per cent sodium bicarbonate in 1 per cent glucose	0.546gm. per 42.5c.cm.
1 per cent glucose	0.484gm. per 46.9c.cm.
5 per cent glucose	0.258gm. per 11.8c.cm.
0.5 per cent glucose	0.098gm. per 42.4c.cm.
0.5 per cent sodium bicarbonate in 5 per cent glucose	0.075gm. per 4.05c.cm.

Chloride and calcium determinations were run on the inorganic salts in most of the experiments of the fifth series. As may be expected, the hypotonic sodium chloride solutions showed an increase in chloride content in a majority of the determinations. Calcium on the other hand consistently was absorbed from the commercial water solution although the absorption took place in only minimal quantities.

Urinary excretion was followed in the first two groups of acute experiments. As may be seen from the accompanying tables, the latter showed no correlation to the amount of fluid absorbed. It was first thought that this was due to the method of administration of the hypnotic employed but it was not the case. It may be that the hypnotic in such doses had a deleterious effect in the kidneys or that the water balance of the blood and tissue was disturbed by the narcosis or that the peritoneal effusion following the trauma of experimental procedure accounted for the remainder, but this is doubtful. In order to come to some conclusion, we decided to follow the urinary excretion in our experiments in chronic conditions. The results will be discussed in that section.

In the first series an effort was made to determine whether the absorbed solutions had any effect upon the water content of the blood. To this end control samples of blood were withdrawn from the animals before the experiment and at the end of each run. The samples were weighed and allowed to evapo-

TABLE IV—SERIES 2, URINARY EXCRETION

Solution used		Experiment No.										Total ave.
		1	2	3	4	5	6	7	8	9	10	
1 Per cent glucose	c.cm.	3.0	1.0	7.0	4.0	6.0	8.0	5.0	2.0	10.0	8.0	6.4
	pt.	2	1	4	3	5	5	2	3	4	3	3.2
.5 Per cent $CaCl_2$	c.cm.	6.0	1.5	5.0	7.0	6.0	3.0	12.0	1.0	1.0	7.0	4.95
	pt.	4	2	2	5	5	1	4	2	1	2	2.8
.7 Per cent NaCl	c.cm.	2.0	4.0	6.0	5.0	5.0	5.0	5.0	9.0	8.0	13.0	6.1
	pt.	1	5	3	4	4	3	2	5	3	4	3.4
Locke's	c.cm.	4.0	2.0	11.0	0.0	2.0	7.0	14.0	6.0	12.0	8.0	6.6
	pt.	3	3	5	1	3	4	5	4	5	3	3.6
5 Per cent glucose	c.cm.	10.0	3.0	2.0	1.0	1.0	4.0	11.0	0.0	7.0	16.0	5.7
	pt.	5	4	1	2	2	2	3	1	2	5	2.7

rate their water content to a constant weight, the process covering 3 days. The water content of the serum plus corpuscles did vary but the results were not comparable with the absorption. In other words a solution which was relatively slowly absorbed from the bowel might show a greater water content in the blood than one which was far better absorbed from the gut. We shall attempt in this connection to make no explanation for the results.

Again, we noted no correlation between the size of the animal and the amount of the fluid absorbed. One would expect that in the larger animals with potentially a greater absorptive area, one would see a greater absorption but despite this we have noted some of the best absorption in our smallest animals. This factor may be explained on the basis of the animal's intake before the experimental periods.

Results on unanæsthetized dog experiments. Series 8 and 9 consisted of 6 experiments on each four animals, the best absorbed solutions in the inorganic salts and glucose concentrations of series 5 and 6 being used. The results indicated that 1 per cent glucose is better absorbed than either 0.5 per cent glucose or 0.5 per cent sodium bicarbonate in 1 per cent glucose. The data suggest that the 1 per cent solution comes closer to the physiological optimum point than the others and that the addition of 0.5 per cent sodium bicarbonate may raise the total osmotic tension beyond the optimum level. The findings were totally in keeping with those of the acute experiments. The data on the inorganic salt runs indicated that the 0.5 per cent sodium bicarbonate solution was slightly better absorbed than the other two solutions, making the 0.5 per cent sodium chloride the second in order whereas it had been first in the acute runs by a small margin.

As we have suggested earlier, it was decided to follow the urinary excretion in the animals with chronic conditions to determine whether this ran parallel with the absorption. Our results indicate that it does not. No attempt was made to govern the water intake of the animals because it was realized that if we had to give them enemas as was necessary under the conditions of the experiments, we would introduce a great deal of error. The animals evidently absorbed water up to the point of tissue saturation before any increased excretion took place. This process did not seem to have any correlation with the comparative rate of absorption—did not affect the latter. The urinary acidity went down almost invariably as would be expected due to the dilution. The latter was measured by titration with fortieth normal sodium hydroxide and phenolphthalein.

The tabulated results of the experiments in the chronic conditions in Table X appear later. It must be remembered that here we are dealing with solutions whose concentrations are uniformly low so that the differences will not be as striking as though the concentrations were widely divergent.

TABLE V.—SERIES 3

Solution used		Experiment No.										Total ave.
		1	2	3	4	5	6	7	8	9	10	
Kalak	c.cm.	16.0	18.0	20.0	16.0	11.5	20.0	17.0	28.0	15.0	20.0	18.15
	pt.	5	4	4	4	5	5	4	5	3	4	4.3
Dist. HOH	c.cm.	14.0	20.0	26.0	12.5	9.0	16.0	21.0	16.0	18.0	23.0	17.55
	pt.	4	5	5	3	4	4	5	3	4	5	4.2
½ Per cent $NaHCO_3$ in 1 per cent glucose	c.cm.	11.0	16.0	20.0	19.0	5.0	13.0	16.0	19.0	21.0	19.0	15.9
	pt.	3	3	4	5	3	3	3	4	5	3	3.6
2 Per cent $NaHCO_3$	c.cm.	−8.0	4.0	3.0	−2.0	−15.0	−10.0	−11.0	−17.0	−12.0	−21.0	−8.9
	pt.	2	2	2	2	2	2	2	2	2	2	2.0
2 Per cent $NaHCO_3$ in 5 per cent glucose	c.cm.	−14.0	−26.0	−19.0	−23.0	−23.0	−37.0	−35.0	−33.0	−34.0	−37.0	−28.1
	pt.	1	1	1	1	1	1	1	1	1	1	1.0

TABLE VI.—SERIES 4

Solution used		Experiment No.										Total ave.
		1	2	3	4	5	6	7	8	9	10	
.5 Per cent glucose	c.cm.	34.0	16.0	25.0	33.0	35.0	28.0	31.0	28.0	23.0	27.0	28.0
	pt.	5	4	5	5	5	4	4	4	4	5	4.5
10 Per cent dextrin in .9 per cent NaCl	c.cm.	15.0	17.0	21.0	20.0	18.0	29.0	33.0	30.0	24.0	10.0	23.0
	pt.	3	5	4	4	4	5	5	5	5	3	4.3
½ Per cent $NaHCO_3$ in 5 per cent glucose	c.cm.	16.0	2.0	4.0	2.0	−7.0	1.0	10.0	5.0	3.0	11.0	5.4
	pt.	4	3	3	3	3	3	3	3	3	4	3.1
Dextrin sol.	c.cm.	10.0	0.0	3.0	1.0	−9.0	−2.0	8.0	4.0	2.0	10.0	2.7
	pt.	2	2	2	2	2	2	2	2	2	2	2.0
Peptone sol.	c.cm.	−27.0	−23.0	−31.0	−28.0	−37.0	−33.0	−6.0	−9.0	−6.0	0.0	−20.0
	pt.	1	1	1	1	1	1	1	1	1	1	1.0

EXPERIMENTS ON MAN

It was early realized that if our suggestions were to have any clinical application, our experiments would have to be carried out in part on the human. We further appreciated that the introduction of a given amount of fluid into the rectum was simple enough but that many obstacles lay in the way of an accurate measurement of the amount of fluid absorbed in a stated period of time. Hence we could not definitely say whether some fluid had not been retained in the crypts of the bowel at the end of a run, when it was siphoned off for measurement, or whether some had not gone past the ileocolic sphincter. However, in 55 cases tested at St. Luke's Hospital, we noted results almost completely in accord with our work on dogs. Our experimental periods necessarily had to be lengthened to minimize the experimental error. To this end we ran 12 hours on each solution, allowing the individual patient 12 hours of rest. Only 2 solutions could thus be compared on each patient in the period of his hospitalization. The patients chosen ranged from those practically normal to those who had had major operations. Of the many patients so treated in the hospital, there were several outstanding cases. For purposes of illustration it may be well to give a short résumé of 2 and to discuss the third in detail because of the opportunity given us for accurate study.

CASE 1. The patient, a middle aged woman, had had several thoracoplasties performed upon her because of an extensive pulmonary tuberculosis. Her condition became very poor following her last operation and resort was made to hypodermoclysis and proctoclysis because of her inability to retain fluids given by mouth. Physiological saline procto-

TABLE VII.—SERIES 5

Solution used		Experiment No.										Total ave.
		1	2	3	4	5	6	7	8	9	10	
.5 Per cent $CaCl_2$	c.cm.	48.0	15.0	29.0	21.0	50.0	13.0	70.0	32.0	35.0	16.0	32.6
	pt.	5	5	4	5	5	2	5	1	3	4	3.9
.5 Per cent $NaHCO_3$	c.cm.	45.0	15.0	29.0	19.0	42.0	15.0	70.0	37.0	30.0	18.0	32.0
	pt.	3	5	4	4	3	3	5	4	2	5	3.8
Kalak HOH	c.cm.	47.0	10.0	39.0	11.0	43.0	17.0	64.0	35.0	30.0	18.0	31.4
	pt.	4	4	5	1	4	4	4	3	2	5	3.6
.7 Per cent NaCl	c.cm.	36.0	+6.0	21.0	17.5	40.0	13.0	41.0	33.0	53.0	18.0	28.45
	pt.	2	1	2	3	1	2	3	2	5	5	2.6
Tap HOH	c.cm.	31.0	+2.0	25.0	12.5	41.0	18.0	40.0	44.0	38.0	15.0	26.25
	pt.	1	2	3	2	2	5	2	5	4	3	2.9

TABLE VIII.—SERIES 6

Solution used		Experiment No.										Total ave.
		1	2	3	4	5	6	7	8	9	10	
.5 Per cent glucose	c.cm.	30.0	27.5	52.5	30.0	45.0	53.0	39.0	51.0	52.0	32.0	42.5
	pt.	4	4	4	4	5	3	4	4	3	3	3.8
1 Per cent glucose	c.cm.	26.0	35.5	57.0	45.0	42.0	59.0	40.0	56.0	70.0	44.0	46.85
	pt.	3	5	5	5	4	4	5	5	4	5	4.5
5 Per cent glucose	c.cm.	11.5	8.0	14.0	4.5	13.0	14.0	4.0	18.0	21.0	10.0	11.8
	pt.	2	3	2	2	2	2	2	2	2	2	2.1
½ Per cent $NaHCO_3$ in 1 per cent glucose	c.cm.	33.5	27.5	30.0	34.0	39.0	76.0	28.0	51.0	71.0	35.0	42.5
	pt.	5	4	3	3	3	5	3	4	5	4	4.3
½ Per cent $NaHCO_3$ in 5 per cent glucose	c.cm.	7.5	3.5	6.0	1.5	7.0	5.0	+1.0	+4.0	7.0	8.0	4.05
	pt.	1	2	1	1	1	1	1	1	1	1	1.1
Dist. HOH	c.cm.		29.0	27.0	38.0	26.0	43.0	42.0	46.0	46.0	33.0	36.6

clysis was not retained although repeatedly tried. Administration of 1 per cent glucose by rectum resulted in the absorption of 1320 cubic centimeters of fluid in 12 hours. Patient at this time was comatose and died before further experiments could be made.

CASE 2. A boy, aged 12 years, was brought into the hospital suffering from an acute exacerbation of lymphatic leukæmia. Any effort to administer fluids by mouth was promptly followed by emesis. He was absolutely unable to retain physiological saline or 5 per cent glucose proctoclysis and refused to submit to intravenous infusion or hypodermoclysis. In the first 24 hours on 1 per cent glucose proctoclysis he absorbed 2300 cubic centimeters of fluid without any discomfort. He received fluids (1 per cent glucose) over a period of days in the same manner—until he could again retain them when given by mouth.

Through the kindness and co-operation of Doctors L. L. and S. W. McArthur we were able to secure one patient upon whom an accurate study could be made.

CASE 3. This man had come into the hospital 6 months previously with an acute obstruction of the bowel which was localized in the left transverse colon. He had been operated upon and a cancerous growth had been removed. His recovery had been uneventful and he had been discharged. His return to the hospital was due to a recurring acute obstruction. A barium enema disclosed the fact that the old tumor site was again involved in a mass which completely shut off the bowel. An ileocolostomy was performed which sutured the ileum to the descending colon below the site of the tumor. The ileum had previously been cut and tied off by pursestring sutures at its junction with the colon. A colostomy opening was made to the surface from the blind loop of gut so formed. The conditions then were excellent for an accurate study on the loop of gut. The patient's recovery was practically normal. He was attended by day and night nurses so that the subsequent experi-

TABLE IX.—GLUCOSE ABSORPTIONS IN SERIES 6

Solution used		Experiment No.										Total ave.
		1	2	3	4	5	6	7	8	9	10	
.5 Per cent glucose	mgm.	.224	.1763	.171	.1688	.2005	.205	.204	+.691	.3596	+.036	.098
	pt.	1	1	3	1	2	2	1	1	4	3	1.9
1 Per cent glucose	mgm.	1.032	.7536	.8236	.248	.5674	.352	.645	.010	.288	.124	.484
	pt.	4	5	4	3	4	4	4	4	3	4	4.0
5 Per cent glucose	mgm.	1.6115	.432	+.059	.2384	.081	.100	1.044	.208	+.652	+.480	.258
	pt.	5	3	2	2	1	1	5	5	1	1	2.6
½ Per cent $NaHCO_3$ in 1 per cent glucose	mgm.	.891	.752	.830	.4264	.729	.408	.588	+.0707	.468	.436	.546
	pt.	3	4	5	5	5	5	3	3	5	5	4.3
½ Per cent $NaHCO_3$ in 5 per cent glucose	mgm.	.4225	.227	+1.6	.2605	.532	.345	.396	+.519	+.417	+.393	+.075
	pt.	2	2	1	4	3	3	2	2	2	2	2.3
Dog weights		8.58K.	6.3K.	11.4K.	6.4K.	13.5K.	15.4K.	6.3K.	15.6K.	15.5K.	8.3K.	10.73

ments were made continuous. A thermos can was employed in this case, as in the others observed at the hospital. The can was suspended from an adjustable stand which was operated by a crank. A tube on the side of the container allowed one to see the height to which the given solution filled the latter. It was then a simple matter to see that the pressure remained constant. The pressure again was just sufficient to overcome the intra-abdominal pressure. The time interval chosen was 4 hours for each solution. At the end of such a period the fluid was siphoned out and a comparison between the amount with which we started the experiment and that we finished with, gave us the total absorbed. The bowel was washed out after each experiment with warm tap water. Six tests therefore were made each 24 hours, the 2 solutions being alternated. As a glance at the charts of series 10 will show that our results were again in accord with those in our dog work.

It must be noted that although Table XI shows that 1 per cent glucose was run first every day, this was not so; it was alternated precisely as the solutions in the other experiments. The chart was so made for simplicity.

Especial note must be made of the fact that the patient whom the above experiments were performed on was under no fluid limitation as far as the oral route was concerned. Hence the total amounts absorbed must be necessarily less than they would be if this was the only source of fluid and the patient was dehydrated. The patient's main complaint was his frequent necessity to void large quantities of urine.

ANALYSIS OF RESULTS

Calcium solutions. At the time that this work was initiated, it was suggested that on the basis of the generally known depressant action of the calcium ion that it might be of interest to observe what the effect of a low concentration of the latter would be upon the rate of its absorption from the colon and to compare this with other standard solutions. In earlier work, the writer, working with J. S. Rozen on the antagonism of calcium and magnesium in the gut, was able to demonstrate increased activity in the isolated stomach strip by bathing the latter in 0.05 per cent calcium chloride, over that which had been elicited by Locke's solution. We noted at that time that if we increased the concentration of the calcium to 0.5 per cent, rigor ensued which remained over a period of hours without a return of activity when bathed with Locke's.

Contrary to our expectations, the 0.5 per cent calcium chloride was one of our best absorbed solutions. In an attempt to arrive at the mechanism involved, the rectal manometer set up was used. The kymographic records of 3 experiments indicated that the gut was actually depressed as far as peristalsis was concerned, but that the absorption was independent of the depression.

Sodium chloride solutions. Of the sodium chloride solutions, the 0.7 per cent was by far the best. It, however, was not quite as readily absorbed as the tap water which had a very low chloride content. The 0.9 per cent sodium chloride was one of the poorest solutions that we dealt with. The composition of the Ringer's solution that we used was 0.7 per cent

TABLE X.—RESULTS IN CHRONIC CONDITIONS

Solution used	1st run c. cm.	2nd run c. cm.	Total absorbed c. cm.
1 Per cent glucose	432	812	1244
0.5 Per cent glucose	521	460	981
1 Per cent glucose	721	789	1510
1 Per cent glucose and 0.5 per cent sodium bicarbonate	709	654	1363
0.5 Per cent glucose	677	729	1406
0.5 Per cent sodium bicarbonate and 1 per cent glucose	858	660	1518
0.5 Per cent sodium bicarbonate	836	785	1623
Com'l water	758	753	1511
0.5 Per cent sodium bicarbonate	746	596	1342
0.5 Per cent sodium chloride	470	602	1072
0.5 Per cent sodium chloride	940	364	1304
Com' l water	844	436	1280

sodium chloride, 0.03 per cent potassium chloride, and 0.025 per cent calcium chloride. The principal constituent here is the 0.7 per cent sodium chloride and as may be readily noted by comparison of series 1, 2, and 5, the results are closely similar. Locke's solution on the other hand, having nearly the same quantity of sodium chloride in it that the physiological saline has, gives results very similar to the latter. The Locke's solution used was that originally proposed by the author.

Tap water and distilled water. Tap water was shown to be superior to both the 0.7 sodium chloride and the Ringer's solutions to about the same degree, although the actual comparison of all three does not take place in any one series. Experimentally, the tap water was also far better than the 0.9 per cent sodium chloride. In 7 of 7 experiments in series 5, the tap water showed an increased chlorine content. The 0.7 per cent sodium chloride also illustrated the same phenomenon so that we may possibly assume that the results were explainable on the basis of a difference of the osmotic pressure of the bowel and the bowel content causing an extravasation of the chlorine ion into the bowel and the absorption of the water content of the clyster to equalize the pressure.

TABLE XI.—RESULTS OF CONTROLLED EXPERIMENTS ON MAN

SERIES 10.—GLUCOSE SOLUTIONS

Solutions used	Experiment number					Total 1 per cent c.cm.	Total 5 per cent c.cm.
	1	2	3	4	5		
1 Per cent	300	340	900	700	750	2990	
5 Per cent	550	180	400	780	440		2350
1 Per cent	580	420	540	560	780	2880	
5 Per cent	600	420	120	600	200		1940
1 Per cent		520	700	610	930	2760	
5 Per cent		400	500	140	660		1700

Total 1 per cent glucose 8630c.cm. Total 5 per cent glucose 5990c.cm.

We had no adequate reason for running experiments on both the tap and the distilled water save that the latter was rarely used clinically. We make no distinction between their comparative merits.

Dextrin and peptone solutions. Fantus, in his "Technique of Medication," in the portion devoted to nutrient enemas, suggests the possibilities of using dextrin as a nutrient constituent because of its non-irritability and ease of conversion into dextrose by the diastase of the bowel. He further suggests that this substance be made up in 0.9 per cent sodium chloride to adjust the osmotic tension. He quotes Carl Von Noorden for his formulæ for two other nutrient enemas, one of which is carbohydrate mainly and the other of which has a peptone base. The composition of the 3 is given in the first part of the paper.

These 3 solutions were compared with 2 glucose solutions in series 4. The peptone was exceedingly hydroscopic.

Protein digestions indicated that absorption of from 700 to 900 milligrams/250 cubic centimeters of solution had taken place in our interval of 45 minutes. This was not a quantitative finding, however, because of the presence of a great deal of mucus—evidently secreted by the bowel as a defense mechanism against the infused irritant.

Of the 3 solutions, the dextrin in 0.9 per cent sodium chloride showed the best absorption of fluid, possibly explained on the basis of the water content. The results are fairly close to those of the 0.9 per cent sodium chloride alone. The fate of the dextrin solution was impossible to note because of the insolubility which made

TABLE XII.—SODIUM BICARBONATE SOLUTIONS

	c.cm.
1 Per cent sodium bicarbonate	450
½ Per cent sodium bicarbonate	620
1 Per cent sodium bicarbonate	500
½ Per cent sodium bicarbonate	310
1 Per cent sodium bicarbonate	260
½ Per cent sodium bicarbonate	660

Total ½ per cent sodium bicarbonate 1590c.cm. Total 1 per cent sodium bicarbonate 1210c.cm.

TABLE XIII.—TAP WATER AND NORMAL SALT SOLUTION

	c.cm.
Tap water	600
0.9 Per cent sodium chloride	500
Tap water	600
0.9 Per cent sodium chloride	370
Tap water	500
0.9 Per cent sodium chloride	320

Total tap water, 1700c.cm. Total 0.9 per cent sodium chloride 1190c.cm.

TABLE XIV.—GLUCOSE AND SODIUM BICARBONATE SOLUTIONS

	c.cm.
5 Per cent glucose and 2 per cent sodium bicarbonate	0.00
1 Per cent glucose and ½ per cent sodium bicarbonate	500.00
5 Per cent glucose and 2 per cent sodium bicarbonate	420.00
1 Per cent glucose and ½ per cent sodium bicarbonate	180.00
5 Per cent glucose and 2 per cent sodium bicarbonate	0.00
1 Per cent glucose and ½ per cent sodium bicarbonate	220.00

Total 1 per cent glucose 900c.cm. Total 5 per cent glucose 420c.cm

TABLE XV.—TAP WATER AND SODIUM BICARBONATE SOLUTIONS

	c.cm.	c.cm.
Tap water	0.0	700.0
½ Per cent sodium bicarbonate	700.0	640.0
Tap water	400.0	500.0
½ Per cent sodium bicarbonate	400.0	600.0
Tap water	440.0	540.0
½ Per cent sodium bicarbonate	500.0	400.0

Total ½ per cent sodium bicarbonate 3240c.cm. Total tap water 2440c.cm.

it necessary to use a suspension rather than a solution.

Glucose solutions. Clinically it has been noted that the patient empties his bowel occasionally, when submitted to a glucose proctoclyster over a period of some time. This phenomenon has been ascribed to the fact that the solution becomes "irritating." The proper interpretation is hard to determine but presumably a mass reflex is initiated which causes an emptying movement. This is usually in regard to the 5 per cent solution. We have noted that these solutions are definitely hygroscopic. It would seem then that under the present method of clysis (the drip method), there would be a constant piling up of the fluid pressure within the bowel with additional fluid coming into the latter from the blood. The bowel is, in this fashion, prevented from diluting the glucose to the point where it is readily absorbed and the resultant distention of the gut causes a mass peristalsis. There is little doubt that the higher concentrations are irritating for we have noted *repeatedly* that the fluid returned from the bowel in both dog and human is clouded with mucus. It will be noted further that as the concentration of glucose goes up, the rate of absorption of both solvent and solute goes down. This is especially noticeable in studying the 1 per cent and 5 per cent solutions. The 0.5 per cent glucose, however, has less water and less dextrose absorbed from it than the 1 per cent, so it appears that we are dealing with a slope to and from the latter. This makes it evident in any circumstances that the theoretical concentration for an optimum solution (5.2 to 5.4 per cent—Fantus) is far too high.

We are puzzled by the fact that some of the solutions showed a higher sugar concentration at the end of a run than at the beginning. This seems to be independent of the concentration and of the order in which the solutions were run. It is not a hangover from the previously run solution because it appeared as well in the first experimental run on 2 days—when the previously run distilled water showed no dextrose content. Distilled water was run as the first solution in 9 out of 10 experiments to determine whether there were reducing substances in the bowel—and though the water was returned distinctly yellow in several cases, due to the fæcal material, we were never able to get a positive test for sugar. The latter tests were run on the sixth series. Two experiments were controlled in the same fashion in the fourth series with the same results.

All sugar determinations were made by the Folin-Wu colormetric method. The 0.5 per cent, 1 per cent, and 5 per cent glucose solutions were not made up to the exact concentrations by analysis because it was felt that slight variations in the concentrations would lead us to a better knowledge of what actually occurred. These small variations had no apparent effect upon the results. The glucose

determination results on the chronic animals and on the human were of the same order as those obtained in the acute experiments.

Since no attempt was made to separate the inorganic salt solutions from the nutrients in the early series we gained an accurate standard of comparison of the relative rate of absorption of the two types of substances. In series 2, the 1 per cent glucose was definitely better absorbed than the 0.5 per cent calcium chloride and the 0.7 per cent sodium chloride. In series 3 the 0.5 per cent sodium bicarbonate in 1 per cent glucose was slightly less absorbed than the commercial product and distilled water. We prefer, however, to accept the results gained in series 6 on the basis that the differences here are more striking in the average amounts of fluids absorbed as well as in the total amounts. Here we note that the 1 per cent glucose with and without bicarbonate and the 0.5 per cent glucose are all more readily absorbed than the distilled water. *We can then perhaps come to the tentative conclusion that 1 per cent glucose solution is the ideal for restoring water balance and for supplying some degree of nutrient.*

High glucose concentrations. In our previous experiments we had come to the conclusion that high glucose concentrations defeated their own purposes by the tremendous hygroscopic effects which they displayed. We had been advised of the use of 25 per cent glucose as a small retention enema in chosen cases and were, therefore, desirous of knowing the fate of such a solution. To this end we ran a series of 3 acute experiments on dogs. Varying from our customary procedure we ran the animals on this concentration *only* for a period of 3 hours. The time then was four times as long as the usual one. We believed that perhaps some glucose would be absorbed as the dilution was increased by the bowel. Records were made of the colon contractions during 1 hour periods on each dog. The record made on the second dog of the series displayed the most interesting results. The tracing showed enormous excursions of the manometer which were readily comparable with those of the unanæsthetized animal and several records of what we assumed were emptying movements when observed in the normal animal. At least the normal dog would show uneasiness which was concurrent with a high contraction and a reflux of the solution back into the bottle. The glucose solutions are here again assumed to be irritating because of the large amount of mucus noted in the fluid drained off after the experiment.

Two of the 3 animals were under very light anæsthesia and the third was in a state of shock from overdosage of barbital, yet all results were in the same order.

The animals weighed respectively, 7.4 kilograms, 7.8 kilograms, and 20 kilograms. The first animal (the one in shock) showed an increase of 73 cubic centimeters of fluid over that which was run into the bowel, the second showed 135 cubic centimeters increase, and the third showed an increase of 255 cubic centimeters. These figures become striking if, taking the total blood of the animal as being one-thirteenth of its body weight, we see that we have removed one-fifth of the figure. If it is possible to apply the analogy of dog to human, we see that a man weighing four times that of the latter dog's weight would have lost in the 3 hours, 1020 cubic centimeters of fluid. Under these circumstances, it is extremely interesting to determine what this solution would do in those patients suffering from myocardial or renal deficiency. As a proctoclyster the solution seems to be useless.

Sodium bicarbonate solutions. Examination of the accompanying tables will bring out the fact that the ionic concentration of the salt plays a great part in its rate of absorption; that is, as the concentration of a salt goes up the quantity of solvent absorbed per unit time, goes down. Thus the 0.5 per cent sodium bicarbonate solution shows a far greater absorptiveness than the 1 per cent (about two times as good), while the 2 per cent is definitely hygroscopic.

As is indicated elsewhere, the bicarbonate solutions were run in combination with the glucose in varying concentrations. In all instances the addition of the former slowed up the rate of absorption of the latter.

The commercial water was used in this series of experiments because of its reputation as an alkalinizer and due to its use by a few surgeons as a proctoclyster. Those who had

intimate knowledge of its use were enthusiastic about it to the extent that they prescribed it for those patients that were unable to retain the classical clysters and stated that it was much better retained than those they were accustomed to use routinely. The results which we had with the solution were very favorable, and may be explained on the basis of its salt concentration. It must be remembered that most of the calcium in this solution precipitates out at body temperature as the insoluble carbonate.

CONCLUSIONS

1. The rôle of proctoclysis is in the establishment and maintenance of water balance in selected cases where it is impossible or inadvisable to administer fluids by mouth. It is used rather than hypodermoclysis or intravenous infusion in any but acute conditions and in conjunction with those methods in the latter. It is our contention that such administration of fluid is thoroughly adequate and physiological.

2. One per cent glucose solution is the most efficient proctoclyster of those studied in this series. It may be combined with 0.5 per cent sodium bicarbonate with a somewhat lowered rate of absorption, but a possible greater effect in combating acidosis.

3. Of the inorganic salts studied, 0.5 per cent sodium bicarbonate solutions were superior to others in rate of absorption.

4. Isotonicity is not the ideal concentration for a given solution for by maintaining such a concentration we are neglecting one of the best properties of the gut; its action as a semipermeable membrane. Hence if we introduce a solution definitely hypotonic to the blood it is more readily absorbed—following the laws of osmosis. In regard to the glucose solutions we may consider that the selective activity of the gut cells comes into play.

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THE INCIDENCE OF TETANUS BACILLI IN THE STOOLS AND ON THE REGIONAL SKIN OF ONE HUNDRED URBAN HERNIOTOMY CASES[1]

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POSTOPERATIVE tetanus has for many years constituted one of the most dreaded surgical complications. In spite of the recent advances in asepsis and operative technique, cases of tetanus following various surgical procedures are still occasionally encountered. Even the most rigorous precautions and meticulous attention to asepsis may be insufficient to prevent the unwelcome appearance of lockjaw. The experience from time to time of having a patient die following a relatively simple, elective operation, as for instance herniotomy, leads one to develop a dread of the tetanus bacillus. The sheer helplessness of the operator once lockjaw appears, leads him to consider even the advisability of routine administration of prophylactic doses of tetanus antitoxin. Obviously it is far more desirable to determine the source of infection and to eliminate it if possible. The present study was undertaken with this object primarily in view.

The great diversity of operations and the wide variation in incubation periods in connection with postoperative tetanus is well illustrated in a historical and statistical review of the subject. Wilms, 1868–1879, placed on record 5 cases of tetanus following herniotomy. Olshausen, 1886, collected 49 cases of tetanus following ovariotomy. Pizzini, 1898, isolated tetanus bacilli from the pus, fæces, and the appendix of a 25 year old individual who died of tetanus. Koch, 1898, related a case that had been operated upon for myoma of the uterus. The patient developed tetanus on the sixth day and died on the seventh. Tourneau, 1904, described three cases of tetanus, one of which followed herniotomy. The patient convalesced uneventfully until the ninth day when tetanus set in, causing death. Zaccharias, 1908, reported 2 cases of tetanus following gynecological operations. One of his patients recovered while the other died on the third day following the onset of tetanus. Richardson, 1909, published 2 of his own cases of postoperative tetanus. In the first case, 6 days after a gall-bladder operation, tetanus developed and caused death within 48 hours. In the second case, operation was performed for strangulation of omental tissue in the sac of a right inguinal hernia. The patient recovered and left the hospital after 14 days. A week later signs of tetanus appeared and the patient died 2 days later. The same author recorded 21 other postoperative cases of tetanus which were operated upon for the following cause or procedure: ovarian cyst, 4; hysterectomy, 4; radical cure of hernia, 4; gall stones, 3; acute appendicitis, 1; acute pancreatitis, 1; carcinoma of the rectum, 1; varicosities, 1; and scirrhus of the breast, 1. Eighteen of these 21 patients died.

Reinhard and Assini, 1909, described a case of tetanus which developed 10 days after a herniotomy and ended fatally within 3 days. Natonek, 1914, gave a complete review of the literature of various types and sources of tetanus infections. Speed reviewed the literature of postoperative tetanus up to 1916 and described 6 cases, 2 of which were observed in the Cook County Hospital, Chicago. His cases are as follows: In Case 1, hysterectomy, salpingo-oophorectomy, and appendectomy were done and 11 days after the operation evidence of tetanus appeared and resulted in death. In Case 2 an inguinal herniotomy was performed and secondary hæmorrhage followed. Tetanus developed 9 days after the operation and ended fatally. In Case 3, tetanus developed 15 days after a cholecystectomy and caused death. In Case 4, cholecystostomy with drainage was done and tetanus appeared 7 days later and led to

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death. In Case 5, the patient was dismissed from the hospital 12 days after a bilateral inguinal herniotomy but returned 6 days later with tetanus. A small pus pocket was found in the left inguinal region. Energetic treatment with tetanus antitoxin was instituted immediately and the patient recovered. In Case 6, a left sided inguinal hernia, tetanus developed 11 days after the operation and ended fatally. The autopsy revealed one deep suture which had passed through the wall of the sigmoid. Smears and cultures of the exudate showed tetanus bacilli. Tulloch, 1919, recorded 2 cases of tetanus which developed following abdominal operations, 1 an appendectomy and the other the reduction of an intussusception. Huggins, 1920, cited a fatal case of tetanus which developed 8 days after a hysterectomy. In spite of vigorous treatment with tetanus antitoxin the patient expired within 48 hours. Murstad, 1921, reported 4 cases of postoperative tetanus, 2 supravaginal hysterectomies, 1 appendectomy, and 1 nephrectomy. Wohlgemuth, 1923, observed 2 cases of postoperative tetanus each supervening upon resection of the small intestine. Evidence of tetanus appeared on the fifth and tenth days following operation.

Records of cases of postoperative tetanus indicate that the largest number develop subsequent to lower abdominal operations especially in the rectal, genital, and pelvic regions. This observation has led to the incrimination of the intestinal tract as a source of infection. Matas, as early as 1910, pointed out that infection occurred through the fæces and therefore he advised abstinence from raw fruits and vegetables as well as thorough cleansing of the intestinal tract 3 to 4 days prior to operation. In 2 cases of postoperative tetanus which he observed, the patients partook freely of uncooked vegetables 24 to 36 hours prior to operation. Huggins agreed that the intestinal tract was the source of infection and advised, in addition to abstinence from raw fruits and vegetables, the administration of a strong purge preliminary to operation. Tulloch also substantiated the contention of Matas that the intestinal tract is the source of infection in tetanus following abdominal operations. In one of his cases of tetanus following an appendectomy, tetanus bacilli were isolated from the wound in the abdominal wall, from the stump of the appendix, and from the fæces in the descending colon.

That the intestinal tract may be the source of contamination of abdominal wounds is indicated by the incidence of tetanus bacilli in the intestinal tract, wounds, and lesions developing between the digestive tract and the abdominal wall. Pizzini isolated tetanus bacilli from the fæces, pus, and appendix of a 25 year old individual who died of tetanus. This author claimed that the infection had taken place through the intestine. Reinhard and Assini, in their fatal case following herniotomy, isolated tetanus bacilli from the pus of the wound the day of onset of the lockjaw. Tetanus bacilli were subsequently recovered from the inguinal lymph glands, heart's blood, lungs, liver, spleen, and kidneys. Speed isolated tetanus bacilli from the exudate of a deep stitch which was passed through the wall of the sigmoid during an inguinal herniotomy. Tulloch described 2 cases of tetanus following abdominal operations in both of which the infection was intestinal in origin. In the first case, that of an appendectomy, tetanus bacilli were isolated from the wound, the abdominal wall, the stump of the appendix, and the fæces in the descending colon. The organisms proved virulent for animals. In the second case in which an intussusception was reduced, material from the wound and fæces revealed tetanus bacilli. The same author, during his extensive work on war wounds found that 20 per cent of wounds of men showing no clinical evidence of lockjaw contained tetanus bacilli at some time during the process of repair. He concluded that the degree of tissue devitalization is the determining factor in the growth of tetanus bacilli and that this devitalization may be produced by bacillus welchii toxin. According to him, tetanus bacilli may be found long after the infection of the wound (882 days in 1 case). Van der Reis found almost a pure culture of tetanus bacilli in the lower ileum and cæcum of a patient with secondary anæmia who suffered from neither tetanus or abdominal distress. These organisms were highly pathogenic to animals.

Tetanus bacilli are much more common in the stools of rural people who come in contact with soil, domestic animals, horses, cattle, etc., than in urban people. Ten Broeck and Bauer found about one-third of the population in the vicinity of Peiping harboring tetanus bacilli in the digestive tract. They claim that tetanus bacilli grow in the intestinal tract, for one individual may eliminate several million tetanus spores in a single stool. Buzello and Rahmel, in Germany, examined 50 rural cases (46 men and 4 women) for the presence of tetanus bacilli in the fæces. These people were normally engaged on farms. Of these 50 individuals 20, or 40 per cent, showed tetanus bacilli in the stools without showing any symptoms of tetanus or ever having had the disease. The authors claim that a previous injection of tetanus antitoxin had no effect upon their findings. Kahn, in his investigation of anaerobic flora in 72 individuals in New York City, found none containing tetanus spores. He concludes that New York City lacks an adequate medium for such infection, whereas in China, where night soil is used for fertilizing purposes, tetanus bacilli and carriers of tetanus spores are much more widespread. Fildes examined fæces from 200 persons in England and isolated tetanus bacilli from 2. Bauer and Meyer, in their study of human intestinal carriers of tetanus spores in California, found that 24.6 per cent gave positive results. Most of the individuals examined, however, were not natives of California, but their nationality is not given. Bauer and Meyer contend that tetanus is more prevalent in California than in Eastern United States and quote statistics of the State Board of Health of California which for the period of January 1, 1922, to December 1, 1925, include 245 cases of tetanus with a mortality of 67 per cent. Szymonovicz, 1929, agrees with other workers that carriers of tetanus bacilli are largely among rural people as well as among cavalrymen.

This study was undertaken in the hope of finding the percentage of carriers of tetanus bacilli in stools and on the regional skin of 100 herniotomy cases in Chicago and vicinity where, according to the literature, no such study has ever been made.

METHOD

The method of culturing adopted was that suggested by Dr. Ivan C. Hall in a personal interview. The inguinal region as well as the umbilicus were swabbed with a sterile cotton applicator, 1 per cent dextrose veal infusion broth being used. A specimen of fæces was also collected. A small representative portion of the stool was thoroughly emulsified, cultured aerobically, and then each emulsified specimen was divided into two portions, one of which was heated at 80 degrees C. for 20 minutes to kill the non-spore-bearing organisms. Cultures of the unheated as well as of the heated specimens of fæces and skin washings were made in deep 0.1 per cent dextrose brain broth sealed with sterile vaseline. These heated and unheated cultures were made at Dr. Hall's suggestion because occasionally only vegetative tetanus bacilli are found which are killed upon heating at 80 degrees C. for 20 minutes. The cultures were incubated for 7 days and Gram stains made at the end of 48 hours and after 7 days. Cultures showing Gram positive bacilli with terminal spores (tetanus-like bacilli) were subcultured by withdrawing 1 cubic centimeter of material from the bottom of the tube and making deep 0.1 per cent dextrose agar shake cultures. This was done with cultures which previously had been heated, while those which had not been heated before were heated at 80 degrees C. for 20 minutes prior to making deep agar shake cultures. Aerobic plates were also made to test for the presence of aerobic organisms.

The deep agar shake cultures were made in tubes especially prepared for this work. They consisted of glass tubing about $\frac{3}{3}$ inch in diameter and about 8 inches long with rubber corks at the base and cotton plugs in the usual manner.

These cultures were observed daily for 7 days. Then the bottom of the tubes was gently warmed, the rubber stoppers withdrawn, and the column of agar permitted to drop into sterile petri dishes. The agar was cut into small pieces with a sterile scalpel and ten colonies were picked from each culture and inoculated into separate tubes of 0.1 per cent dextrose brain broth. After incubation for 5 to 7 days Gram stains were made and toxicity

tests performed on all cultures showing tetanus-like organisms by subcutaneous injection into guinea pigs of 0.1 cubic centimeter of the culture.

All abdominal washings which showed bacillus welchii-like organisms were subcultured and tested for stormy fermentation of litmus-milk and against rabbits in the usual manner.

Results. Of the one hundred individuals examined none of the skin washings revealed any tetanus bacilli either before or after surgical preparation. Only one of the stools yielded tetanus bacilli which were pathogenic for guinea pigs. With regard to other anaerobic organisms five of the cases showed bacillus welchii on the skin before preparation and two additional cases after preparation, furnishing a total of seven. The aerobic organisms isolated from the skin in these one hundred surgical cases are:

A. Before preparation for operation—
Bacillus subtilis in 5 cases.
Staphylococcus aureus in 15 cases.
Staphylococcus albus in 31 cases.
Streptococcus hæmolyticus in 2 cases.
Diphtheroid bacillus in 28 cases.
Pneumococcus in 2 cases.
Micrococcus catarrhalis in 8 cases.
Bacillus coli in 3 cases.
Bacillus mucosus capsulatus in 4 cases.
Streptococcus viridans in 13 cases.
Staphylococcus albus hæmolyticus in 4 cases.
Staphylococcus aureus hæmolyticus in 1 case.
Sarcina lutea in 1 case.

B. After preparation for operation—
Bacillus subtilis in 4 cases.
Staphylococcus aureus in 2 cases.
Staphylococcus albus in 7 cases.
Streptococcus hæmolyticus in 1 case.
Diphtheroid bacillus in 7 cases.
Pneumococcus in 2 cases.
Micrococcus tetragenes in 1 case.
Bacillus coli in 1 case.
Streptococcus viridans in 2 cases.

DEDUCTIONS FROM STUDY

It is evident from the foregoing that the mode of life, occupation, etc., play a rôle in the degree of infestation with tetanus bacilli. The rural people who are engaged in farming and who are in more or less constant contact with the soil, cattle, horses, and various other animals show a higher percentage of infestation with tetanus bacilli than the urban professional and industrial people. In China where night soil is used for fertilization, about ⅓ of the people show tetanus bacilli in the stools.

In California similarly high results have been obtained by Bauer and Meyer most of whose work has been done on people who are not natives of California, but whose nationality is not mentioned. In reports from England there is a wide discrepancy among the results obtained by various workers. Kerrin, after examining a large number of individuals, did not find any carriers. Fildes found 1 per cent while Tulloch, after examining the stools of 21 overseas men and 31 civilians, found 7 positive for tetanus bacilli among the former and 5 among the latter. He also found 20 per cent of war wounds of men showing no evidence of tetanus, harboring tetanus bacilli at some time during the process of repair.

The difference in the percentages of positive carriers is probably best explained on the basis of the type of individuals examined, whether urban or rural. In Germany, Buzello and Rahmel examined 50 rural persons who were engaged on farms and in contact with horses and cattle. They found that 40 per cent of this group were carriers of tetanus bacilli. In Poland, Szymonovicz also found a higher percentage of carriers of tetanus bacilli among rural people who were engaged in farming and among cavalry men than among urban people. In this country the results of Bauer and Meyer for California are very high, viz., 24.6 per cent. In New York City, Kahn in his investigation of the anaerobic flora in stools of 72 individuals failed to find any tetanus bacilli.

In our investigation of the stools, and the umbilical and inguinal regions of 100 herniotomy cases at the Cook County Hospital, Chicago, we found only one carrier of tetanus bacilli in the stool and recovered none from the skin. However, we have found that skin contamination with bacillus welchii as well as with aerobic pathogenic bacteria is very common. Since bacillus welchii in association with aerobic bacteria is a very efficient tissue devitalizer it follows that should any tetanus bacilli gain entrance into the wound or skin about the region of the wound, they would find fertile ground for propagation and the production of tetanus.

CONCLUSIONS

1. The stools of healthy individuals not infrequently contain tetanus organisms.

2. A fair percentage of individuals harbor on the skin adequate tissue devitalizing organisms (bacillus welchii in combination with pathogenic aerobic bacteria) even after the usual routine surgical preparation.

3. The occurrence of postoperative tetanus in cases in which exogenous sources (catgut, etc.) can be excluded are to be traced to organisms derived from the intestinal tract.

4. Stool and regional skin cultures should constitute part of the routine search for the source of contamination in all cases of postoperative tetanus.

5. The incidence of healthy carriers of the bacillus tetanus is relatively high among the rural population and relatively low among urbanites (1 per cent in Chicago).

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THE ETIOLOGY OF PLACENTA PRÆVIA

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ALTHOUGH placenta prævia is regarded as a very dangerous complication of pregnancy, when sufficient care is taken the mortality should be practically nil. In the first 4 years of the present Mastership, there were 78 cases with no death. In spite of these good results, the condition is one to avoid when possible and anything which suggests a method of avoiding a repetition of the disease must be seized upon with avidity. We are carrying out clinical and experimental investigations, the results of which we hope to publish in due course.

In a paper read before the British Medical Association in 1929 by one of us (B.S.), the known theories were mentioned, and the remark was made: "A pathological condition of the endometrium is a fruitful cause of placenta prævia. Curettage should be done before the next pregnancy." In the practice of the author, there has never been a "repeat" case.

We must now reiterate that it is quite unreasonable to imagine that the ovum can indulge in a uterine abortion after which it is to acquire new life again. Theories, other than these, which suggest some pathological condition of the endometrium bear no close scrutiny.

From animal experiments conducted by one of us (H.E.C.), and from observations on the non-pregnant uterus, we believe that the cause of placenta prævia lies in a defective or deficient production of the decidua formation of the upper portion of the uterus, with a normal or sufficient amount of decidua in the lower portion of the uterus. When the fertilized ovum, therefore, enters the uterus, it will seek the place where it can obtain the greatest amount of nourishment. Since the upper portion is deficient or poorly developed to receive the tenant it will be attracted to the greatest amount of decidua reaction—in the lower portion of the uterus.

The factors which predispose to deficient decidua formation are those which diminish the stroma of the endometrium thus replacing it by fibrous tissue, e.g., infections, frequent pregnancies. It is known that the amount of decidua reaction will depend upon the cellular structure of the endometrium, that is, the more cellular the greater the production of the decidua. Changes in the endometrium as to diminution of the stroma cells occur more readily in the upper portion than in the lower. There is, therefore, no deficiency of stroma cells in the lower portion, so that there should be a normal amount of decidua production when pregnancy occurs.

In a normal uterus, the amount and thickness of the decidua is uniform and when a fertilized ovum enters the uterus it will implant itself immediately in the upper portion, as there is no need to look for a better site. But when the upper portion is deficient, then for physiological reasons, that is, in order to continue its growth, it must obtain better nourishment, it will look for a better location.

If a rabbit's horn is traumatized (by passing a needle through) and allowed to become pregnant, pregnancy in that horn is most unlikely to occur. If the upper portion only is traumatized and the lower one left is free and the rabbit is allowed to fall into pregnancy or pseudo-pregnancy, the greatest amount of congestion will occur in the non-traumatized area. Thus we may conclude that by traumatizing the endometrium we destroy the stroma and probably in those parts fibrous tissue takes its place and the latter is a poor producer of decidua formation.

SUMMARY

A new theory for the causation of placenta prævia is suggested: it is entirely plausible, is borne out by experiments on animals and by clinical observations.

CLINICAL SURGERY

FROM THE ROYAL HUNGARIAN UNIVERSITY

RADIUM TREATMENT OF CANCER OF THE CORPUS UTERI

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OPINION as to the value of radium in the treatment of cancer of the corpus uteri is as yet not uniform. According to the majority of workers, cancer of the corpus uteri, because of the organ's low grade sensibility to radiation, does not as a rule respond favorably to radium therapy. Other authors, however, report most gratifying results.

At the First Gynecologic Clinic of the University of Budapest between 1919 and 1920, 101 cases of cancer of the corpus uteri have been observed. Of these 45 were treated by means of radiation therapy, the other 56 by operation. With this large number of relatively carefully observed and followed up cases, we shall try to give an exhaustive discussion of this question.

Cancer of the body of the uterus is found less frequently than cancer of the cervix; it represents about 10 per cent of all cancers of the female genital organs. Most patients with cancers of the corpus uteri have passed the menopause. Cancer of the corpus uteri is most frequently encountered between the fifth and sixth decades; it is not a rarity, however, even in later decades. The age incidence in our cases is shown in Table I.

TABLE I.—AGE INCIDENCE IN CANCER OF CORPUS UTERI

Ages in years	Cases
20 to 30	0
30 to 40	5
40 to 50	29
50 to 60	40
60 to 70	23
70 to 80	4

The youngest patient in this series was 34 years, the oldest 75 years of age. In addition to the greater frequency at the more advanced age, there is another difference between cancer of the corpus and of the cervix in that the latter is relatively more prevalent in nulliparous women. In our series there were 38 nulliparæ, 2 of whom were virgins, 14 primiparæ, and 49 multiparæ.

The most important symptoms are irregular bleeding and a bloody, foul discharge. Irregular bleeding in older patients, especially after the menopause, should arouse the suspicion of the presence of cancer of the corpus uteri. Pain is a later symptom; as a rule it indicates the encroachment of the tumor upon the surrounding tissues. Diagnosis can be made by uterine scraping and microscopic examination of the tissue removed—enlargement and softer consistency of the uterus, bleeding, and discharge, which are generally observed, cannot be accepted as sufficient evidence of the presence of this disease; nor are uterine sound findings reliable diagnostic criteria.

On microscopic examination cancer of the corpus uteri usually has the appearance of adenocarcinoma, more seldom that of solid carcinoma. In our series there were 86 instances of adenocarcinoma, 13 instances of solid carcinoma, and 2 instances of carcinosarcoma. According to many contributors the prognosis in a given case depends to a certain extent on the histological character of the tissue. In general, it may be said that adenocarcinoma is more radioresistant than is solid cancer. When the cancer involves the corpus uteri, the prognosis is more favorable than when the growth involves any other part of the female genital tract, owing to the fact that the process remains for a relatively long time localized in the body of the uterus. The thick muscular wall of the uterus protects the parametrium and surrounding organs from encroachment, so that their involvement is a late complication. Remote metastases are rather unusual.

For cancer of the corpus uteri, there are two types of treatment; surgical removal and radiation treatment. As cancers of the corpus uteri are localized in character, they offer a favorable field for surgical treatment. Several authors report as high as 80 per cent operability, whereas in cancer of the cervix the operability generally does

not exceed 25 per cent. Simple vaginal hysterectomy usually suffices; more extensive operations are seldom necessary. Laparotomy is done only in the presence of complications, such as large fibroids or inflammatory tumors of the adnexa. The high operability percentage and the fact that less extensive operations are required so that the operative mortality rate is low explain the empiric fact that surgical treatment of cancer of the uterine corpus yields much better results, both relative and absolute, than those obtained in the surgical treatment of cancer of the cervix. Collective statistical data on cancer of the corpus uteri show about 50 per cent of surgical cures.

At the First Gynecologic Clinic of the University of Budapest, of 101 cases of cancer of the corpus uteri observed during 10 years, 56 were operable, 56.5 per cent. Of the 28 cases observed for more than 5 years, 12 were cured, 42.9 per cent. There were 3 deaths, thus making the operative mortality rate 5.3 per cent. Owing to its high percentage of operability and to the favorable results in such treatment of cancer of the body of the uterus, surgical treatment is naturally preferred. In general, only cases inoperable in the anatomical and clinical sense of the word are referred for radiation therapy. To the cases inoperable from an anatomical standpoint, because of the widespread extension of the disease, there must be added a great number which are clinically inoperable because of advanced age, poor general health, or some other complication, all of which tend to make the patient a bad surgical risk.

In the radiation treatment of cancer of the corpus uteri, we combine radium with the X-ray. Radium is used for local treatment, but for the parametrium and the lymph glands, high voltage radiation is used. The latter is used also in the postoperative treatment. Before radium tubes are introduced, the cervical canal must be dilated. When radium tubes are being placed in the uterine cavity, the utmost care must be used—instruments and other material must be sterilized—in order to avoid untoward complications, sometimes ascribed to radium therapy. Septic complications after the application of radium in the treatment of cancer of the corpus uteri, as a rule, result from forced dilatation of the cervical canal. In the carcinomatous tissue, masses of virulent streptococci can be demonstrated, so that even a most insignificant laceration may give rise to a septic process. If the cancerous growth is so large or so situated as to make dilatation difficult, it is better not to use force to produce dilatation but, for the present, to insert the radium tube in the vagina. Such an application of radium may cause the growth to disappear or at least the virulency of the bacteria to be reduced. After this preliminary preparation and after the vagina has been irrigated with a disinfectant, the conditions are much more favorable for an attempt to dilate the cervical canal. Uterine sound examination furnishes orientation as to the shape and size of the uterine cavity. The cervical canal is carefully dilated by means of metal dilators. The cervical canal must be dilated to a diameter larger than that of the radium tube in order to secure, during treatment, sufficient drainage of the discharge; a rise in temperature during the intra-uterine application of radium is often due to retention of secretions. For the insertion of radium tubes into the uterine cavity, usually curved rubber sheaths, which are available in various lengths and which can be easily sterilized, are employed.

The radium should not remain in the uterine cavity more than 48 hours. If fever or chills occur, the radium tube must be removed at once. The required dosage can be given by applying the tubes for short periods at a time, at intervals of a few days. The technique of radium irradiation in the treatment of uterine cancer has not undergone appreciable change except that the utmost care as to application and asepsis must be used. It is due to these efforts that in most cases the danger from the spread of infection can be eliminated. In order to complete intra-uterine radium irradiation, it is expedient to combine it with the vaginal application of radium. In the treatment of the parametrium and the lymph glands, external radiation is employed; usually the X-ray is used or in institutes which have larger quantities of radium at their disposal, the external application of radium at a distance is used.

The results of radiation therapy in cancer of the corpus uteri may be shown chiefly by means of the collective statistics of Seitz and Heyman. Seitz reports 233 cases in which cure was effected by radiation treatment in 78, or 34 per cent. Heyman reports 271 cases, both operable and inoperable, and in these cures are reported in 91, or 47.5 per cent. Against these favorable results in operable cases—results which nearly equal the results of surgical treatment—we find the outlook for radiation therapy much less favorable in the inoperable cases. In cancer of the corpus uteri the results in radiation therapy are unfavorably influenced by the low grade sensibility of adenocarcinoma to radiation and by the fact that as it is difficult to be certain as to the exact location of

the neoplastic focus, we are unable to regulate the distance at which the radium tubes should be placed to give adequate irradiation. The latter circumstance is a great hindrance in those cases in which there are complications from uterine fibroids, which are found in about 25 per cent of the cases. In cancer of the corpus, a relatively small number of patients is inoperable because of the great extension of the process; advanced age, general debility, and concomitant diseases often contra-indicate surgical intervention. In inoperable cases radiation therapy is the only method of treatment.

In our series of 101 cases, 45, or 45.5 per cent, were inoperable. Patients unsuitable for operation were referred for combined radiation treatment. The intra-uterine application of radium is accomplished with the utmost care; great precautions are taken to prevent infection. Fortunately, in our series, no severe infections have been observed. During the course of treatment two patients had high fevers which subsided after the radium tubes were removed and the patients rested for a few days.

In the uterine cavity usually we apply 50 to 75 milligrams of radium, which is enclosed in silver or brass tubes of a thickness equivalent to a filter of 1 millimeter of platinum, and these tubes are placed in a sterilized capsule. If possible, the total dosage of 2,400 to 3,600 milligram hours is administered at one sitting. More recently we have completed the intra-uterine application by giving 2,000 to 2,400 milligram hours of radium through the vagina. For external irradiation the X-ray is employed; three times through from two to six portals of entry—three-fourths of a skin erythema dose per portal, which is equal to 470 r. measured in air. The apparatus consists of a radiotransverter machine, Coolidge tube, 185 kilovolts, 5 milliampères, ½ millimeter zinc plus ½ millimeter aluminum filter, 30 centimeter focal skin distance. Patients who have received radiation therapy are re-examined at first every 6 weeks, later every 3 months, and then every 6 months, respectively. To those who do not appear for re-examination questionnaires are sent.

Of 45 patients with inoperable cancer of the uterine corpus treated by means of radiation therapy, 26 were under observation for more than 5 years. The duration of life after treatment is shown in Table II. One each was free from recurrence for 6, 7, and 8 years, respectively, and these three are still under observation. There are therefore 4 cases of 5 year cures, 15.3 per cent. Of 19 cases observed for less than 5 years, there are free of recurrence 1 for 4 years; 2 for 3 years; 1 for 2 years, and 2 for less than 2 years.

TABLE II.—DURATION OF LIFE AFTER TREATMENT

Years after treatment	Cases
Less than 1	9
1	5
2	7
3	1
4	0
5	1
6	1
7	1
8	1

In the medical literature, among others who have published the results which they have obtained in radiation therapy in rather large series of cases of cancer of the corpus uteri are Amreich, Bumm, Doederlein, Eymer, Gál, Heyman, Lacassagne, Lehoczky-Semmelweiss, Schmitz, Seitz, Voltz, Ward, Wintz, and Zweifel.

The problem of radiation therapy in cancer of the body of the uterus cannot be regarded as definitely solved. With added experience, however, we would seem to be justified in the hope that further development and improvement in radiation therapy will lead to results far superior to those so far obtained.

FROM THE VANDERBILT UNIVERSITY, SCHOOL OF MEDICINE

AN EASY OPERATION FOR THE REMOVAL OF CANCER OF THE RECTUM IN THE FEMALE[1]

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THE object of this communication is to call attention to an operation for the removal of cancer of the rectum in the female. The operation was first performed in 1890. In 1900, John B. Murphy read a paper before the Southern Surgical and Gynecological Association, at its meeting in Atlanta, entitled "Resection of the Rectum *per Vaginam*." This paper was published in the *Philadelphia Medical Journal*, February, 1901. Murphy did not remove the whole rectum as is carried out in the modern operation. He resected it and brought the two ends of gut together, using long interrupted silk sutures which were brought out through the anus. In nearly every one of his cases rectovaginal fistula followed and was repaired at a subsequent operation. Murphy reported 5 cases without a death and reviewed the literature up to that time. His paper gave the impetus which in time evolved the modern operation.

It is of interest to note that cancer is still on the increase among civilized nations, but rare in tribal communities. Gant says that he has never observed a case of cancer of the rectum in the American negro although he has maintained several clinics for this race. His explanation of this immunity is that tuberculosis and syphilis are prevalent in this race and that these diseases render them immune. This can not, however, explain the infrequency of carcinoma of the rectum in the American negro as all of them have not syphilis or tuberculosis. Williams' table shows in 7,327 cases of organic cancer that the rectum was involved in females in 4.3 per cent and in males in 7.5 per cent of the cases. Nothnagel in 343 autopsy specimens of intestinal carcinoma reports that 164 involved the colon and 162 the rectum. Gant's statistics show that the frequency of involvement of the various parts of the rectum in the 300 cases are as follows, rectosigmoid, 15 per cent; upper rectum, 20 per cent; ampulla, 50 per cent; anal canal, 10 per cent; and anus, 5 per cent. The etiology is unknown but it is of importance and interest to remember that benign tumors of the rectum are potentially dangerous and in the majority of instances are transformed into malignant growths in the course of time. F. W. Rankin (6) has recently published a paper which strongly emphasizes this point and shows concrete examples of neoplasms, innocent in character, being transformed into carcinoma. The symptoms I will not attempt to review as they are well known. The diagnosis is easily made if one will only make a rectal examination in every case that presents anal or rectal symptoms. It is a reflection on the surgeons of this country that cancers of the rectum in many instances are first operated on for hæmorrhoids and the cancer is not discovered until another examination is made subsequent to the hæmorrhoidectomy due to the persistence of symptoms.

I emphasize to the senior students each year in my course in gynecology that any medical man in any city or hamlet regardless of his training can make a diagnosis of cancer of the cervix or rectum by a simple vaginal or rectal examination and prove it by biopsy, should these examinations show anything of a suspicious nature.

I am firmly convinced that in women, regardless of age, rectal symptoms should call for a digital or proctoscopic examination and that a biopsy should be done if occasion demands it. The operation that I am about to describe is applicable only to cancers of the rectum in females. It is ideal where the growth is in the lower rectum or ampulla and in the upper end of the rectum, provided it is not too far advanced, and some advise its use in cancer of the rectosigmoid. With this latter view I am not in accord and would advise, in rectosigmoid cancers, following the method advised by Jones, Lahey, Rankin (5), or Coffey, all of whom have read before this Society papers which are landmarks in surgery of the large intestine.

The following case is a rather typical example of this condition and well illustrates the points I desire to emphasize.

Mrs. A. T. W., aged 59 years, consulted me March 12, 1929. She was the mother of 7 children, the youngest 22 years of age; she also had one premature child. The family history was of no importance. For more than a year before she consulted me she had noticed a bearing down

[1] Read before the Southern Surgical Association, White Sulphur Springs, West Virginia, December 9, 1931.

sensation in the rectum which was followed in a few months by the passage of a small amount of blood. She was constipated but did not take purgatives regularly. During the last 6 months she had lost 25 pounds. She had a good appetite and digestion and slept well. She had had no past illnesses of any importance except that 10 years ago her gall bladder had been removed and following this she developed a phlebitis of the left lower extremity. A physical examination showed the patient to be in good condition. Pelvic examination showed a relaxed vaginal outlet with the uterus normal in size and position and no enlargement of the appendages. At the upper end of the vagina a mass, a little larger than a walnut, could be palpated in the rectum. The mass could be easily palpated with the index finger. The proctoscopic examination showed the mass to be ulcerating in character and a biopsy specimen proved it to be carcinoma. X-ray examination of chest and spine was negative. The Wassermann and Kahn tests were both negative. Blood pressure was 160-90; hæmoglobin, 75 per cent; red blood cells, 3,500,000; white blood cells, 12,000; weight 124 pounds which was normal for her age and height. The urine contained albumin and many pus cells. She had previously consulted a colleague and friend of mine who had advised a two stage operation with the formation of a permanent colostomy. She had come in intimate contact with a friend of hers who had had a similar operation and stated that she preferred death to a permanent colostomy. She insisted that I try and remove her cancer per vagina as I had previously carried out a vaginal hysterectomy on an acquaintance of hers for carcinoma of the body of the uterus. After the usual pre-operative preparatory treatment the following operation was carried out. Spinal anæsthesia with novocain was used and the patient was placed in the exaggerated lithotomy position. The sphincter was thoroughly dilated,

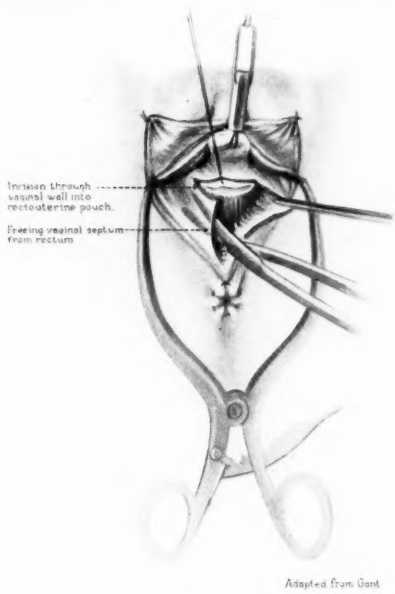

Fig. 1.

Fig. 1. A semicircular incision was made behind the cervix, the peritoneum opened, and a suture passed through it for further identification. The pelvis was then explored by inspection and palpation and gauze packs were placed above the brim to keep the small intestines from getting into the operative field. An incision was then made from the center of the semicircular incision down to within ½ inch of the anus. This incision was carried down to the rectum with care not to buttonhole it. (Adapted from Gant.)

Fig. 2. The superior hæmorrhoidal artery was ligated and divided between double ligatures and the gut divided with cautery between clamps. With the main source of the blood supply ligated and the peritoneum open it was quite easy to detach the upper end of the rectum from the sacrum with the finger, working first in one direction then in another. The mesorectal and lateral ligaments were incised and the rectum separated from vagina by dissection with scissors.

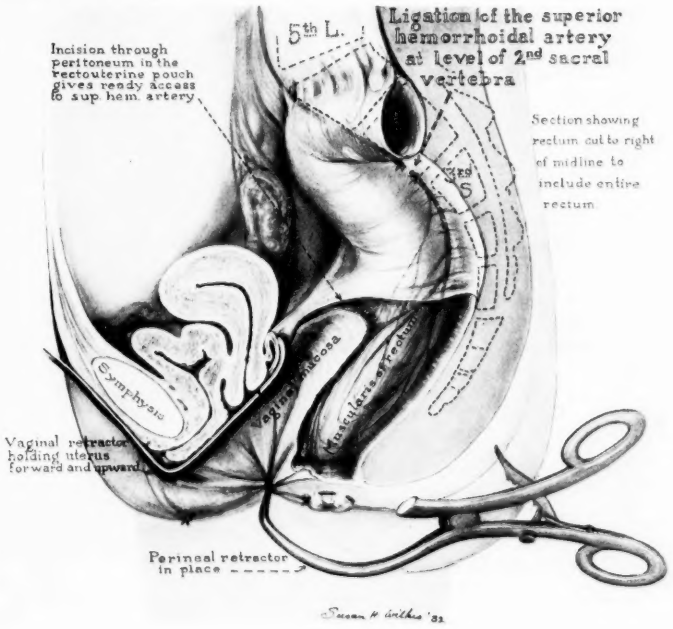
5th L.
Ligation of the superior hemorrhoidal artery at level of 2nd sacral vertebra
Incision through peritoneum in the rectouterine pouch gives ready access to sup. hem. artery
Section showing rectum cut to right of midline to include entire rectum
Sacrum
Symphysis
Vagina
Levator ani
Vaginal retractor holding uterus forward and upward
Perineal retractor in place

Fig. 2.

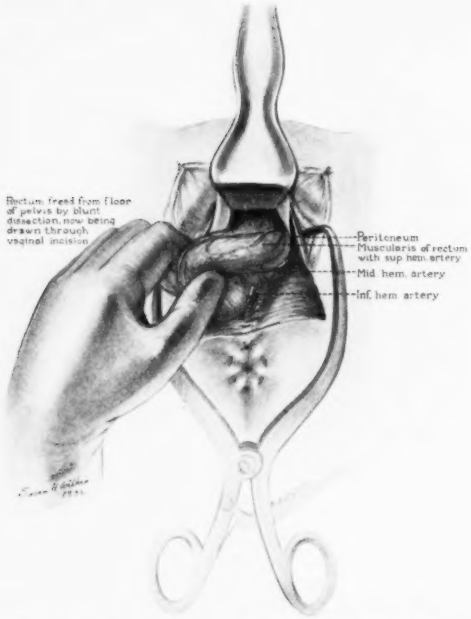
Rectum freed from floor of pelvis by blunt dissection, now being drawn through vaginal incision
Peritoneum
Muscularis of rectum with sup. hem. artery
Mid. hem. artery
Inf. hem. artery

Fig. 3. Oozing was controlled by suitably placed packs, the middle hæmorrhoidal vessels were ligated, and the gut was freed from the levator ani down to the anus. The rectum at the anal canal was then ligated to prevent leakage, incised with cautery, and whole of the rectum which was now detached was lifted out through the vaginal incision.

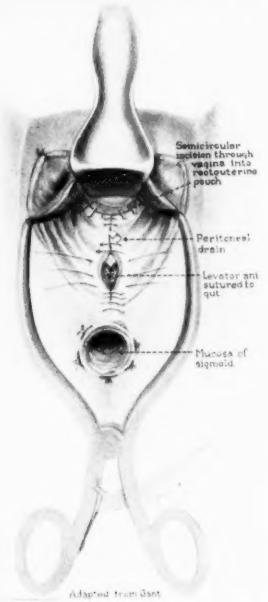
Semicircular incision through vagina into rectouterine pouch
Peritoneal drain
Levator ani sutured to gut
Mucosa of sigmoid
Adapted from Gant

Fig. 4. Shows the sigmoid sutured to the anus from which the mucous membrane has been removed, the closure of the semicircular and longitudinal incision, exit of peritoneal drain and levator ani sutured to gut. (Adapted from Gant.)

the rectum was packed with gauze, and the vagina and external genitals, perianal and perineal regions were scrubbed with soap, water, alcohol, painted with picric acid solution, and the anus closed with a strong suture. The cervix and upper vagina were thoroughly exposed, the cervix seized with hooks and pulled forward. A semicircular incision was made behind the cervix, the peritoneum was opened and a suture was passed through it for further identification. The pelvis was then explored by inspection and palpation and gauze packs were placed above the brim to keep the small intestines from getting into the operative field. An incision was then made from the center of the semicircular incision down to within ½ inch of the anus. This incision was carried down to the rectum, care being used not to buttonhole it. The superior hæmorrhoidal artery was ligated and divided between double ligatures and the gut was divided with cautery between clamps. With the main source of the blood supply ligated and the peritoneum open it was quite easy to detach the upper end of the rectum from the sacrum with the finger, working first in one direction then in another. The mesorectal and lateral ligaments were incised and the rectum was then separated from the vagina by dissection with scissors. Oozing was controlled by suitably placed packs, the middle hæmorrhoidal vessels were ligated, and the gut was freed from the levator ani down to the anus. The rectum at the anal canal was then ligated to prevent leakage, incised with cautery, and the whole of the rectum which was now detached, was lifted out through the vaginal incision. The mucous membrane of the anal canal after being cleansed with a picric acid solution was dissected out and removed. The clamp on the lower end of the sigmoid was then removed, a corrugated tube was placed in its lumen and held there by a silk ligature. It was then brought down, passed through the anus, and sutured to anal margin with interrupted sutures. A drainage tube was then placed in the peritoneal cavity and the peritoneum was closed by suturing it to the gut. At the lower end of the wound, several interrupted sutures of catgut were carried through the levator of one side, the walls of the gut being grasped first and then the levator of the opposite side, and tied. Another tube for drainage was placed below the peritoneal reflection and the vaginal incision was closed. Both drainage tubes were brought out through the vaginal incision in this case, although I can see the necessity under certain conditions of bringing the tube or tubes out through a stab wound. The patient's recovery was free of complications, union was good throughout, she has perfect control of her sphincter muscle and now at the end of 32 months there is no sign of local recurrence or distant metastases.

ADVANTAGES OF OPERATION

The operation described has the following advantages: the function of the sphincter ani is retained and a permanent colostomy is avoided.

The operation provides abundant room and does not weaken the pelvic support. The superior hæmorrhoidal vessels with the peritoneum open can be easily visualized and ligated. Removal of the sacral glands and the division of the lateral and mesorectal ligaments is possible when the gut is being mobilized and the danger of injury to the ureters is avoided. Thorough drainage of all parts of the wound is possible. The operation can be carried out by any surgeon who has had proper general and gynecological training and experience. Spinal anæsthesia was used in this case, and at that time I was most enthusiastic about its use, but time, experience, and laboratory experiments have proved to my mind that it is a dangerous procedure and should be used only in selected cases and when other safer methods are contra-indicated. My reason for this view is that during spinal anæsthesia a vasoconstrictor paralysis occurs. Vasoconstriction is the natural compensating device which nature employs as a corrective for the diminished volume of blood following hæmorrhage and for the low blood pressure subsequent to neurogenic or reflex shock. A mild hæmorrhage may prove fatal if the patient is under spinal anæsthesia.

Gant has a special corrugated tube that screws into a rubber fæcal reservoir that is possibly of some convenience during the period when union of the severed gut is taking place with the anal margin.

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SIX YEARS OF TANNIC ACID TREATMENT OF BURNS

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EVALUATION OF THE RESULTS IN THREE HUNDRED AND TEN CASES SO TREATED

SUFFICIENT time has elapsed since Davidson announced his early observations on the tannic acid treatment of burns in 1925 to justify a consideration of the results thus far obtained. The extensive literature already published on the subject testifies to the fact that the method is being used extensively throughout the world, but it is difficult to find convincing statistics. Most of the observers are enthusiastic about the reduced mortality rates and the comfort of the patients when tannic acid is used.

Unfortunately, burns do not lend themselves well to accurate statistical observations. The extremely variable factors, such as the types of patients received by different hospitals, the marked variation from year to year in the number and character of burns in any given institution, and the difficulty in describing satisfactorily the depth and extent of a given burn all tend to vitiate the value of small groups of statistics. It is only by pooling the results from large groups that any reliable estimate can be made, but such figures are not now available. In the meantime, we must use what criteria we can find.

The group of cases which is the basis of this report, with a very few exceptions, was cared for on the author's service; and in all cases the general procedure for tannic acid treatment adopted by the burn service of St. Luke's Hospital was followed. The 310 consecutive cases included in the report were treated during the 6 years from 1926 to 1931, inclusive. For comparison with this series, all the burn cases treated by various methods, at St. Luke's Hospital from 1922 to 1925, inclusive, were reviewed. More than half of the patients in this group comprising 121 cases were under the care or observation of the author. This fact is mentioned because we feel that it is difficult to evaluate the observations of others.

Effect upon mortality statistics. We have adopted as the criteria of the effectiveness of any method of burn treatment the following: (1) Does it save lives? (2) Is it comfortable to the patient? (3) Does it minimize complications and sequelæ? (4) Does it favor healing? (5) Is it practical and economical?

In answer to the first question, we may say that what statistics are at present available show a marked reduction in mortality from burns when tannic acid treatment is followed. Harris, of Toronto, reports a reduction from 26.6 per cent mortality by other methods to 12 per cent by the tannic acid method. Herzfeld, of Edinburgh, and Wilson report a reduction from 38 per cent to 9 or 9.5 per cent.[1] Beekman, of New York City, found a reduction in mortality from 27.8 per cent to 14.9 per cent; and Bancroft and Rogers, from 40 to 50 per cent to approximately 20 per cent. In the series reported by the author, 121 burns treated by various methods gave a mortality of 14 per cent, while in 310 cases treated by the tannic acid method, the mortality was 9.6 per cent. From these figures it would appear, then, that under the tannic acid regimen the mortality of burns has been reduced from one-half to one-third. The very high mortality figures of 40 per cent to 50 per cent seem unreasonable for any type of treatment, and are probably not representative. The author's figures seem a little low, both for other methods and tannic acid, but this is partly accounted for by the fact that our series was a mixed group of adults and children of all ages (less than 50 per cent were children), while most of the other reported groups were made up almost entirely of children.

The criticism may be made that these apparent improvements in mortality statistics are due to factors in the care of burned patients other than the tannic acid. It must be admitted that, when a group of cases is being studied, the mortality is likely to drop as a result of the greater care in detailed treatment accorded the patients under study. In our series we feel that the treatment other than the use of tannic acid was much the same in both series, with some slight improvement in general therapy during the past decade.[2]

[1] Figures apparently taken from the same hospital series.

[2] We wish to make it clear that we do not regard the series reported here as large enough to be conclusive from the standpoint of mortality statistics. This uncertainty is illustrated by the mortality in our series, if considered by years. In the tannic acid series, the mortality by years was as follows:

Year	Cases	Mortality, per cent
1926	22	0
1927	38	5.2
1928	35	17.1
1929	52	17.3
1930	70	11.4
1931	49	10.2
1927–8 (industrial)	44	0.0
	310	9.6

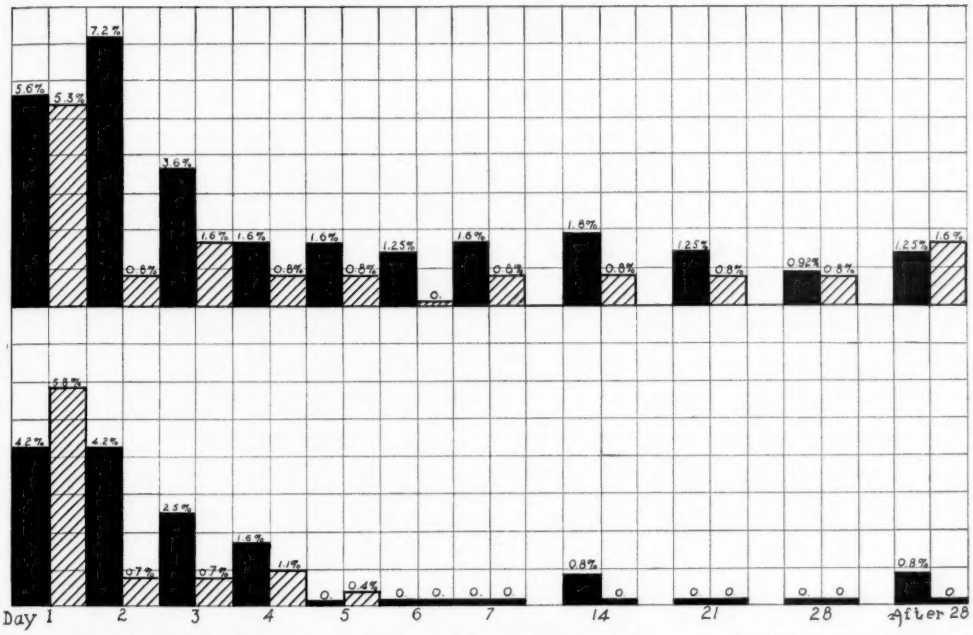

Fig. 1. Graph showing percentage mortality by days in author's series (lower figures) and in series of Beekman (upper figures). The areas with diagonal lines indicate tannic acid treatment, the black areas other methods. The vertical lines indicate days after burn.

More important, perhaps, than the gross mortality rates, is an analysis of the deaths in relation to the various stages of the burn. The accompanying graph shows the percentage mortality by days in the author's series, and those obtained by Beekman, at Belleview Hospital, before and after the use of tannic acid.

It will be noted that during the first 24 hours the mortality rate is much the same regardless of the type of treatment used. The deaths which occur during this stage are due to enormous burns which overwhelm the patient within a few hours. In our series, the patients in this group suffered burns involving anywhere from 50 to 90 per cent of the body surface. In other words, we are completely helpless to save patients of this group with any method of treatment so far devised, and probably will continue to be until the true nature of the death-dealing toxic process is discovered. During the second 24 hour period, however, there is a marked reduction of mortality in the tannic acid treated cases. Here we feel the tannic acid method saves the lives of a certain number of patients who are on the border line and would have been lost under older methods of treatment. There is also a marked reduction in later deaths under the tannic acid regimen. Most of these deaths under older methods of treatment were attributable to infection and septic complications. That these complications are relatively rare with tannic acid treatment, all observers agree, and in our series there was not a single death from infection or septic complication. The 2.3 per cent mortality rate in our series subsequent to the first 48 hours, included 6 deaths in all. Two of these were late toxic deaths, occurring on the third day. The 4 remaining were cardiac deaths occurring on the fourth and fifth days. These will be discussed later.

Comfort of the patient. There can be little doubt in the mind of anyone who has worked with various methods of burn treatment, that tannic acid is comfortable for the patient. After the initial dose of morphine or codeine, which is administered when the patient is admitted to the hospital, frequently no further sedative is required for hours, and in some cases for days, if the tannic acid spray is promptly and efficiently applied. As soon as a firm coagulum has formed over the entire burned area, which usually takes place in from 12 to 24 hours, little attention need be directed to this area, for about a week. During

this time, the patient is relatively comfortable under his lighted cradle-tent (sometimes named by the patient "the covered wagon"), with no cumbersome or painful dressings over the burned areas. Several patients under our care have suffered previous burns which were treated with other methods, and all have been enthusiastic in their praise of tannic acid. No one who has spent tedious hours, painful to the patient and exhausting to both the patient and the physician, doing daily ambrine dressings, will wish to return to such a regimen after a trial of the tannic acid method. To be sure, there is some discomfort connected with the period of separation of the tannic acid coagulum, which begins at the end of the first week. This part of the treatment need not be unduly painful, if continuous dressings wet with Dakin's solution are used, as described subsequently.

Incidence of complications. From the data obtained in our series, as well as the experience of other observers, it would seem that the incidence of septic complications of burns is much lower with the tannic acid treatment than with any other. As previously stated, we had not a single fatal septic complication in our entire group of 310 cases (assuming our interpretation to be correct). In only one case did serious septic complications arise. This was an emaciated child of 3 years, who suffered an extensive burn of both arms, chest, neck, and face, and was treated for 2 days in a small outlying community, before being transported some distance to the hospital. The child developed consecutively, bilateral acute otitis media, bronchopneumonia, and a purulent hip joint infection, but recovered.

We attribute the slight incidence of septic infections in our series to the early removal of the tannic acid coagulum with continuous dressings of Dakin's solution, as soon as exudate begins to form under the coagulum. This deviation from the original technique of Davidson, we consider very important and will be discussed in a subsequent section.

The data at hand concerning other complications are not convincing. In our series we encountered 3 cases of peptic ulcer (2 clearly demonstrated by X-ray), 2 cases of acute cholangitis, 1 case of acute cystitis, 2 cases of acute, polyarticular arthritis, 1 case of peripheral neuritis with paralysis of the common peroneal nerve, and 1 case of retinitis.

The 4 cases which we have classified as cardiac deaths deserve a little explanation. Three of the 4 were children. These deaths occurred on the fourth and fifth day; all had suffered severe burns, but seemed to be well over the dangerous toxic period, with normal pulse rate and practically normal temperature, when they suddenly went into collapse. The clinical picture was much the same in all the cases, and reminded us very much of the late, toxic, cardiac deaths from diphtheria.[1] In each case, the symptoms came on suddenly when the patient appeared to be in excellent condition. The first indications were usually apathy, pallor, and a rising pulse rate, followed by a brief interval of bradycardia, marked irregularity, then vomiting, pulmonary œdema, coma, and death. We have been unable to obtain electrocardiograms in any of these cases, because of the sudden onset of symptoms and the rapidly fatal issue. The patients with severe burns upon whom electrocardiographic observations have been made showed nothing abnormal. We had not observed these phenomena which we have interpreted as being toxic cardiac effects before the days of tannic acid treatment, and we have been inclined to conclude that the patients who develop late cardiac complications under the tannic acid method would not have lived long enough to show these changes under the older methods of treatment.

Effect on healing. In some of the earlier discussions on the tannic acid treatment of burns, considerable enthusiasm was expressed concerning the rôle played by this method of treatment in the healing process, and the opinion was voiced that epithelization took place more rapidly under the tannic acid coagulum than with other types of treatment. It is doubtful if such enthusiasm is entirely justifiable in the light of subsequent experience. It is true that superficial burns in which the basal epithelial layer is not destroyed, will be entirely healed when the coagulum separates off spontaneously at the end of about 2 weeks, but it is equally true that burns of similar depth will be healed in an equal length of time by almost any other method. If the tannic acid treatment has any essential value in favoring healing, it is because secondary infection is less likely to interfere with healing, and this is of great advantage in the deeper burns.

Practical and economical. There can be little doubt that the tannic acid method is practical and economical. The materials required are inexpensive and easily obtainable, and much less tedious care is demanded from nurses and hospital internes than with other types of treatment with which we are familiar, at least during the first week.

[1] The similarity between certain postmortem changes in severe burns and those of diphtheria were noted by Bardeen.

Use in first aid. The criticism is sometimes offered that tannic acid is not practical for first aid in the home or in industry. It is true that there is no preparation of tannic acid which is as convenient to keep or apply at home as are some of the ointments and oils that have been used extensively. If the toxic theory of burns is correct the early treatment is very important. If ointments or oils are applied to the burn in the home or factory before transporting the patient to the hospital, much valuable time is lost in removing these materials with a fat solvent before tannic acid solution can be effectively applied. The tannic acid spray under an improvised lighted canopy can be carried on in the home, but not as satisfactorily as in a hospital. It is becoming generally understood both by the profession and the public that severe burns get along better with hospital care. Tannic acid compresses, re-enforced with a generous layer of absorbent cotton bandaged on, can be applied satisfactorily in the home or factory, will keep the patient comfortable and give him the benefit of the coagulating effect of tannic acid at the earliest possible moment. Tannic acid solution cannot be kept on hand, because it changes to gallic acid during a few days' exposure to light and air, becoming darker in color, and after this it should not be used. The dry powder can be kept indefinitely, however, and to make up a solution of an approximate strength is the work of but a few seconds.

Tannic acid jelly. For 4 years, we have been working with a 5 per cent tannic acid jelly, made up with a tragacanth base about the consistency of the ordinary lubricant jelly, for use in first aid and on ambulatory burn cases. Tannic acid ointment made up with petrolatum or lanolin base is not satisfactory, because not enough of the tannic acid actually reaches the burned surface, and the oily base prevents air from drying the coagulum. The tannic acid jelly has worked fairly satisfactorily, particularly in industrial dispensaries, but has some disadvantages which we have not been able to overcome entirely. The jelly forms a hard coagulum almost as quickly as the tannic acid spray.

Summary. Three hundred and ten consecutive burn cases treated by the tannic acid method are reported, with a mortality of 9.6 per cent. One hundred and twenty-one treated by various methods prior to 1926 gave a mortality of 14 per cent.

The tannic acid method is comfortable to the patient and with it the incidence of complications is low.

It has no essentially beneficial effect on epithelization.

The method is practical and economical.

The Management of Burns with Tannic Acid

The following general outline of treatment is the one we now follow on the burn service of St. Luke's Hospital. The method as originally described by Davidson has been considerably modified, in accordance with our experience. For many details in the management we are indebted to other observers in the field, as well as to the residents and internes on the service whose observations have led to helpful changes in the technique.

Immediate treatment important. Instructions are posted in the accident room of the hospital detailing the treatment of burns. The precedent has been established that burns are to be regarded as emergencies and are to be treated without any delay. In severe burns, we believe that every hour of delay before tannic acid treatment is begun endangers the life of the patient. Experience has led us to believe that the toxic products of the burned tissue absorbed within the first few hours after the burn may determine the outcome. It is, of course, unnecessary to treat all burns as emergencies, but the fallibility of judgment in what constitutes a burn of dangerous degree is so great that, unless all burns are treated in this manner, a serious burn will occasionally be neglected. Even with a fairly large experience with burns, we find it quite impossible to estimate with any degree of accuracy at the outset the extent and depth of a burn. All too frequently a burn in a child is treated by means of some ointment in the home by a physician who regards it as a trivial affair until the second day when the child begins to vomit and have convulsions. The child is then rushed to the hospital at a time when effective treatment may be too late to avoid a fatal issue. These factors have led us to urge the family physician and the interne to regard all burns as serious until proved to the contrary and to give to each patient the benefit of prompt and efficient treatment. We make very little effort to classify burns according to degree or to calculate the area involved in percentages. Attempts to record burns in such manner are misleading and often inaccurate.

The patient is immediately put to bed, without any preliminary formalities in the accident room. He is given morphine by hypodermic, if suffering much pain, and is placed under a lighted cradle, with bedclothes over the cradle in which enough

lights are placed to maintain a temperature of approximately 85 degrees F. Any dressings which may have been applied are removed, and if any grease or oil has been applied to the burned surface this is removed quickly and gently as possible with ether. Vesicles that have already formed are opened with sterile scissors and the outer layers of epithelium which are loose are peeled off. This is important, because unless the badly damaged outer layers are removed, the tannic acid will not coagulate the deeper layers. In the course of the first day, if additional vesicles or bullae form, they should be treated in the same manner. Gross dirt is removed from the wound, but we have found thorough scrubbing with an antiseptic unnecessary and too productive of shock. We have never found it necessary to give the patient an anæsthetic to carry out the procedures just described. With care, this process need not be very painful, and the patient is spared the additional shock and blood concentration resulting from anæsthesia.

Stronger solutions of tannic acid. An aqueous solution of tannic acid (5 per cent for children and 10 per cent for adults) is sprayed over the entire burned area just as soon as the area is prepared (12). We are using the stronger concentrations of tannic acid (2½ per cent was the strength originally recommended by Davidson), because with the stronger solutions, quicker tanning of the damaged tissues is obtained. The more rapidly this is accomplished, the less the toxic absorption and dehydration. The spray from an ordinary atomizer is satisfactory. The tannic acid corrodes the metal parts of the atomizer, however, and usually one or two atomizers are used up in the treatment of each severe burn. Atomizers made entirely of rubber and glass are more satisfactory.

The tannic acid spray is not used on the face. We have experienced no difficulty from injury to the cornea with tannic acid, but rather than risk possible injury to the eye, we have avoided the use of the spray on the face. Instead we have been in the habit of using 5 per cent tannic acid jelly (tragacanth base). This can be spread over the face in a thin layer, which, as it dries, leaves a firm coagulum over the burned areas. This jelly is also used occasionally in certain other inaccessible areas which are difficult to treat with the spray. Petrolatum is smeared about the eyelids, nostrils, and lips to prevent them from becoming uncomfortably dry and stiff, and also in burns of the perineum, it is smeared about the external genitalia and anus.

The tannic acid solution is sprayed over the burned area every hour for the first 24 hours. (In very extensive burns we often spray the areas every 10 or 15 minutes during the first few hours, in order to get the earliest possible coagulation.) If the burned areas are well coagulated and dry at the end of 24 hours, tannic acid spray may be omitted, and no further treatment of the local site of injury will be necessary for several days. During this time, of course, the entire burned surface is left exposed to the air. When skin surfaces must come in contact (as between the arm and the chest wall), a sterile towel is placed between the two. If any part of the burned area must come in contact with the bed, a sterile sheet or sterile towels should be placed under the part. It is usually most satisfactory in large burns, to have sterile sheets placed under the entire body.

Importance of combating dehydration. The most important feature of the constitutional treatment during the early stage of the burn is the administration of an adequate amount of fluid to combat the anhydræmia. In an adult with a burn of moderate extent, an adequate amount of fluid may be taken by mouth, but if he is vomiting or has a very extensive burn it is usually wiser to give the necessary amount of fluid in the form of physiological salt solution or 5 per cent dextrose solution intravenously, per rectum, or by hypodermoclysis. In severe burns, we have been in the habit of giving one intramuscular or intravenous infusion of physiological salt solution and one of 5 per cent dextrose each day, until the toxic manifestations are over. There has been considerable difference of opinion expressed concerning the amount of fluid that should be given, the amount frequently recommended being 100 cubic centimeters a day per kilogram of body weight, although some observers give larger quantities. According to the theories of Underhill and his associates, blood concentration is the cause of most of the toxic symptoms of burns, and the indications are for large quantities of fluid to combat this anhydræmia. It is true that blood concentration takes place almost immediately after a severe burn and continues for a variable time. From clinical observations, however, it is difficult to accept blood concentration resulting from local changes at the site of the burn as the primary lethal factor. It seems more likely that the anhydræmia is merely one of the manifestations of a profound toxæmia, the true nature of which has not yet been determined.

Too much fluid may cause œdema. During the first 48 to 72 hours following the burn, the patient is not able to handle as large an amount of fluid as we formerly believed. It is during this period that the permeability of capillaries throughout the

body, as well as locally at the site of the burn, seems to be greatly increased. Along with this factor, the renal depression, which may be due to œdema of the tubules, renders the individual unable to excrete an unusually large volume of fluid. We have produced generalized œdema in several patients at this stage, with volumes of fluid slightly more than 100 cubic centimeters to a kilogram of body weight. This renal depression seems to last only about 3 days, and after that time the urinary output increases markedly. We have never seen a case of complete renal suppression which we were taught was a common occurrence in severe burns. Likewise, we have never observed any permanent renal damage that has resulted from a severe burn. Theoretically, the continuous intravenous infusion, popularized by Gallie and Harris, Horsley,[1] and others, should be ideal for use in severe burns, but after using it in a number of cases we have discarded the method, except for an occasional case. It is not difficult to produce generalized œdema by this method, in extensive burns. In one young adult, who seemed to be well over the toxic stage of the burn, but suddenly went into collapse and died a few hours after a continuous intravenous infusion had been discontinued, we felt that the amount of fluid administered intravenously had proved too serious a burden to an already handicapped myocardium. At the time the intravenous infusion was stopped, the patient had begun to develop generalized œdema. We have observed only one case of generalized œdema from fluids taken by mouth. This patient had received an extensive burn and demanded large quantities of water, even after he was apparently over the toxic stage. After taking between 6 and 7 liters of fluid per day for several days, he became œdematous. His intake was then limited to 4 liters, and after putting out enormous quantities of urine for several days he recovered his water balance.

Dakin's solution to remove crusts. After the initial temperature rise which usually takes place within the first 24 hours after the burn, the temperature drops to normal or only slightly above when the burned areas have become thoroughly tanned and remains at this level for 5 or 6 days. In the deeper burns, some exudate begins to form beneath the crusts between the sixth and eighth days, as evidenced by a rise in temperature, a sense of fluctuation beneath the crusts, malaise and sometimes delirium. It is at this point that we apply continuous Dakin's solution dressings to loosen up the coagulum as quickly as possible. Large rolls of gauze wet with Dakin's solution are applied to the burned areas, after the normal skin is protected adequately with sterile petrolatum. A heavy layer of sterile absorbent cotton is bandaged over the gauze, and oiled silk is bandaged over all to prevent evaporation, the coagulated areas being kept moist at all times. These dressings are moistened every 4 hours with Dakin's solution, and the entire dressing is changed daily. This type of dressing is continued until the coagulum is all off and the granulating areas are clean and ready to graft or are healing rapidly with epithelial islands that were not destroyed by the burn. The initial application of moist dressings is usually accompanied by a sharp rise in temperature to 39 degrees or 40 degrees C., followed within 24 hours by a drop to between 38 degrees and 39 degrees, and a swinging temperature curve between this level and normal continues until the coagulum and necrotic tissue are all off. If the burn is a superficial one, the coagulum will be off within 3 or 4 days; however, in the deeper burn, where the skin is completely destroyed, it will be in the neighborhood of 2 weeks. It is important that the normal skin included in the dressing be adequately protected with petrolatum; otherwise the constant use of Dakin's solution will cause a painful dermatitis. When the coagulum is off, there remains a granulating wound with or without epithelial islands, and the use of a single layer of bandage gauze impregnated with sterile petrolatum between the granulations and the rolled gauze will render the dressings relatively painless.

The secondary toxic stage. A word of explanation concerning the moist dressings may be in order here, since the practice has been condemned by Davidson, Wilson, and others. In his earlier communications, Davidson insisted that the coagulum be left intact until it separated spontaneously, since upon the integrity of the coagulum depended the protection from toxic absorption. It was his assumption that the period of toxic absorption lasted for a week or more, and that if the coagulum was separated too early, the toxic symptoms would recur. In 2 of his early cases he attempted to separate the crusts prematurely with boric acid compresses, with disastrous results which he attributed to the early removal of the crusts. He had demonstrated the fact that during the first 48 hours following the burn, the blood urea nitrogen, urea nitrogen, and creatinine were elevated and returned to normal as the toxic symptoms abated. He observed that in the 2 cases mentioned, after the crusts were removed by moist compresses, toxic symptoms seemed to return while the nitrogenous products of the blood

[1]Who credits the method to Matas.

again increased. He regarded these findings as indicating that the removal of the coagulum had released more of the toxic products which were present during the first 48 hours. We have not confirmed these observations concerning what we sometimes call the "secondary toxic stage" which comes on usually at the end of the first week following injury, when the coagulum begins to separate. We have found no constant significant changes in blood chemistry determinations made during this stage, but our findings have agreed with those of Davidson during the first 48 hours.

From our interpretation of clinical data we would conclude that the true toxic stage of a burn is over within approximately 48 hours, when efficient tannic acid treatment is started early. When tannic acid is started late, or when other methods of treatment are used, it seems probable that the true toxic stage lasts longer. What we have termed the "secondary toxic stage" coming on at the end of the first week, resembles more the toxæmia of a mild acute infection, or sapræmia. It will be recalled that we have not had a single death during this stage in the tannic acid series (in fact, no deaths after the fifth day), which would tend to confirm our impression that the "secondary toxic stage" is not a continuation of the initial toxic stage during which most of the deaths occur. It seems to us probable that the unfortunate results obtained by some observers may be attributed partly to the absorption of boric acid when the solution is used in large quantities to soften the coagulum, and to its low bacteriocidal properties. Dakin's solution seems to control the symptoms of the "secondary toxic stage" admirably. In some cases, in which it is necessary to continue Dakin's solution over a considerable period of time, patients begin to complain of the burning sensation produced by the antiseptic solution. In such cases, we often substitute physiological salt solution for a few days, and always find that, with the salt solution, the elevation of temperature and symptoms are likely to recur, only to disappear again when Dakin's solution is reapplied.

We feel that it is very important to do everything possible to hasten epithelization of the granulating wound remaining after the tannic acid coagulum is off. During this stage a profound secondary anæmia is likely to develop, and, if long continued, the patient's ability to resist intercurrent infection is impaired. In general, it seems worth while to do some type of skin graft, if the granulating wound is certain to take more than 3 weeks to epithelize after all the coagulum is off and the granulating wound is clean. This is merely a working rule and has its exceptions. During this stage, we have found wet dressings of thiocresol, as described by Reimann, alternating at intervals of 48 hours with physiological salt solution, have a fairly definite tendency to stimulate growth of epithelium. In comparable cases, in which Dakin's solution was used on one extremity and parathiocresol on the other, we have been impressed with the fact that the epithelium grew slightly faster over the areas treated with parathiocresol. There are, of course, many indications for the use of transplants, from the cosmetic and functional standpoint. These will be considered in a later report. Here we merely wish to emphasize the importance of skin grafting to promote early healing and prevent development of a profound secondary anæmia and late septic complications.

Special types of burn. The problems involved in the treatment of chemical burns are essentially the same as those caused by heat. The first indication is for the immediate dilution of the acid or alkali with large quantities of fluid. The chemical is quickly fixed in the tissues, and attempts at neutralization are unnecessary unless the burn is caused by a very concentrated acid or alkali. Flushing the burned area with large quantities of water or normal salt solution is usually adequate to dilute any excess of the chemical remaining. From this point on, the burn may be treated with tannic acid, and the course will be much the same as in the case of a superficial burn from heat.

Some deep burns from concentrated acids or alkalis are not affected by tannic acid, since the superficial tissues are already coagulated by the chemical. This is equally true of small, deep electrical burns. Since the coagulum involves the full thickness of the skin, and sometimes underlying tissues, it separates very slowly. In such cases much time in healing may be saved by doing an immediate excision and skin graft, as advocated by Wells.

Serious burns of the eye are fortunately uncommon, and are usually caused by chemicals. When they do occur the services of a competent ophthalmologist are required. It is astonishing how rarely the cornea is damaged in severe cutaneous burns of the face. The lid reflex apparently is quick enough to prevent damage to the eyeball, in most cases. In chemical burns of the eye immediate flushing of the conjunctival sac with large quantities of sterile water or normal salt solution is important. Only one patient in our series suffered a serious burn of the eye. An alkaline drain compound was the causative agent, and the conjunctiva was completely destroyed,

necessitating enucleation. The reconstruction of the conjunctival sac by means of grafted skin will be described in a later communication.

SUMMARY

A method of management of severe burns with tannic acid is described, the outstanding features of which are:

Burns should be regarded as emergencies and treatment started at the earliest moment.

Burned areas are sprayed with a 5 or 10 per cent tannic acid solution, while the patient remains under a heated cradle.

An adequate amount of fluid is administered to combat dehydration; at the same time care is taken not to overload the circulation with fluid.

Continuous dressings wet with Dakin's solution are used to hasten separation of the coagulum during the "secondary toxic stage." The "secondary toxic stage" is described.

Early skin grafting is recommended to prevent development of a profound secondary anæmia, to diminish danger of late septic complications, and to prevent unnecessary scarring or contracture.

The treatment of chemical or electrical burns involves the same principles as do those caused by heat.

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TECHNIQUE OF PARATHYROIDECTOMY

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SINCE it has been shown that certain forms of osteomalacic conditions, such as osteitis fibrosa cystica, certain forms of ankylosing arthritis and other conditions associated with an increase of the blood calcium are due to tumors, adenomata, or hyperplasias of the parathyroid gland, and since parathyroidectomy in these conditions has given curative results, there can be no doubt that the operation for removal of the parathyroids will be done frequently. Therefore, an outline of its technique as we have applied it in 18 cases, seemed indicated.

Preparation of patients is the same as for other operations on the neck. Some of the patients are very sick from painful deformities and should be properly protected against dehydration. There is no treatment for the hypercalcæmia before operation. The patient should be carefully transported to and placed on the operating table. It has happened that a decalcified bone fractured from improper handling. The stiffened dorsocervical kyphosis of the spine renders exposure of the neck somewhat difficult, but obviously should not be forcibly overcome.

As an *anæsthetic* we prefer gas (analgesia) combined with local ½ per cent novocain, as in goiter. Some have used local anæsthesia alone. At any rate the anæsthesia should be light. Especially when operating around the recurrent laryngeal nerve, it is wise to let the patient talk so that encroachment on the nerve is noticed by interference with phonation and respiration.

Incision. The usual collar incision as in goiter suffices for parathyroidectomy. The straight prethyroid muscles of the neck are separated in the midline from the larynx to the sternal notch and retracted laterally after they are injected and relaxed with novocain. Cutting of the muscles will be only exceptionally necessary in short, kyphotic necks; however, a good exposure is more important than sparing the muscles. Oppel, of Leningrad, who has probably performed more parathyroidectomies than any one else, used a longitudinal incision along the anterior edge of the sternomastoid muscle from the jaw to the sternum. The incision allows exposure of the parathyroids only on one side, but one can never be sure on which side the parathyroidectomy may have to be performed. Only a few parathyroid tumors have been palpated before operation with approximate accuracy. Some tumors palpated before operation proved to be small adenomata of the thyroid. Again, sometimes it is impossible to find the parathyroid on one side when there are not large tumor formations, and one is obliged to remove, on either side, whatever one finds—one or two bodies. Last, it is better to have the whole field exposed so that one, or better two, parathyroids may be preserved. Therefore, the longitudinal incision of Oppel is not to be recommended. In 51 cases in which Oppel presumably had removed a parathyroid, 11 did not show any parathyroid tissue upon microscopic examination. The collar incision should be strictly recommended as the incision of choice, as it allows inspection of both sides.

When the thyroid lobe is properly exposed, it is first inspected on its anterior and lateral surfaces for parathyroids (8 to 9 per cent are located on the anterior, 5 per cent on the lateral surface of the thyroid—Milgram). Then the lobe is gently turned mesial to expose the structures posterior to it. This is best done with fine towel clips which are made to grasp the lobe without injury to the tissue. On the posterior surface the inferior thyroid artery is located between the carotid, *d*, and gland, *t* (see illustration). By teasing apart the fine areolar tissue in this space with 2 fine tissue forceps usually the inferior parathyroid body is readily exposed and recognized by its size, shape, and color. The superior parathyroid lies somewhat higher up, usually at the junction of the upper and middle third of the thyroid edge. A little more blunt dissection of the areolar tissue will expose the recurrent nerve.

If no enlarged parathyroid is found on this side, it is advisable to expose, at this stage, the parathyroids on the other side in the same way. Then one is sure whether there is an actual tumor (adenoma) of the parathyroids present on either side, or if one or several of the bodies are hyperplastic. The decision as to whether the tumors alone should be removed or two or even three parathyroids, is difficult and depends upon two considerations; first, if the symptoms, the hypercalcæmia, the decalcification of bones, is very pronounced and endangers the patient, it is better to remove three rather than two parathyroids. Otherwise two will be sufficient. In case of a definite parathyroid adenoma of 1 centimeter size or more, removal of the same is probably all that is necessary. Second, one should be sure

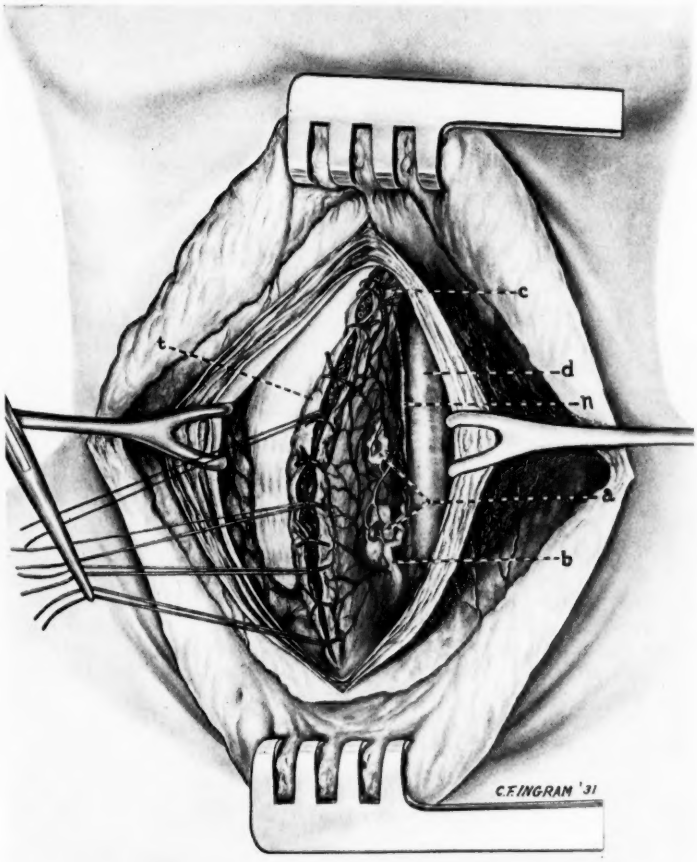

Fig. 1. The left lobe of the thyroid has been subtotally removed. *c*, The ligated upper pole. *t*, Remaining goiter gland bed oversutured; a few guy sutures left long retract the goiter bed mesially exposing parathyroid bodies, *a*. *d*, Carotid and recurring nerve, *n*. *b*, Inferior thyroid artery with a small branch leading into the inferior parathyroid.

that one or two small parathyroids remain to sustain function. It seems that the experience gained in thyroid surgery will repeat itself on the parathyroid. At first surgeons were afraid to remove too much thyroid to avoid postoperative myxœdema—first one-half then three-fifths was the limit, until we learned that it is better to remove too much than too little and the subtotal thyroidectomy was accepted. As myxœdema in surgery of the thyroid, so tetany is the bugbear of parathyroid surgery. In 18 cases of our own, 70 of Oppel's (these, however, unilateral), and 15 cases from the literature, there was only one fatality from postoperative tetany (Beck), and 3, not serious, cases of postoperative tetany (Snapper, Barr, and Bulger, Ballin and Morse). To be sure, we realize that unfortunate complications like postoperative tetany are not always reported. Under proper precautions in technique and the after-treatment outlined, tetany following parathyroidectomy is preventable.

In identifying the parathyroid bodies, remember:

First. There are usually four at the places mentioned, but variations of site are frequent (Terry and Searls).

Second. The color of these epithelial bodies is a yellowish brown according to their fat content or blood content. The most frequent mistakes made have been the removal of small thyroid adenoma, lymph glands, or fat tissue. Thyroid tissue is easily recognized; fat has no resistance to the examining finger; and lymph glands, while yellow-pink, are usually more round and regular in contour. The parathyroids are usually more oblong and stellate, reminiscent of a nerve ganglion. If in doubt a frozen section should answer the question as to whether parathyroid tissue has been removed.

Third. At times identification of the parathyroid has not been accomplished, at least 3 such cases have been confessed to.

Fourth. In some cases primary ligature and division of the inferior thyroid artery will bring the yellowish brown parathyroid into view (E. P. Richardson).

Fifth. Subtotal lobectomy has to be done frequently before the parathyroid can be exposed and removed. Thyroparathyroidectomy is the operation most of the 20 odd surgeons who reported their cases have performed. It has the following advantages before simple parathyroidectomy—it gives better exposure and more space for the delivery and handling of the parathyroids. Some parathyroids are often imbedded in the thyroid and cannot be removed without more or less of a lobectomy (Willburk, 7.8 per cent). Furthermore, the thyroid in parathyroidism is often goitrous and may contribute also to hypercalcæmic and arthritic conditions (Hunter). Therefore, a thyroparathyroidectomy will be preferable in the majority of cases. Only in children, and if the thyroid appears normal and does not interfere with the technique, should the parathyroids be removed alone. (Most of our cases had associated adenomatous goiter.)

After all these points—inspection of both sides of the neck for parathyroids, decision as to how much of them to remove, and subtotal thyroid lobectomy, if needed, has been done—the thyroid lobe or its remnant is drawn mesially and the carotid and muscles laterally (see Fig. 1). At this stage the recurrent nerve should be seen. If necessary after ligature of the inferior thyroid artery, the parathyroid body is lifted up with a fine mosquito forceps, and is freed until its nutritive artery appears starting from the inferior thyroid or from a connecting branch from the superior thyroid. This branch, as well as the inferior, is ligated if necessary, with fine linen or silk (catgut slipped in one of our cases). The body can then be teased out from its areolar fibrous layer without bleeding. The many fine branches providing ample vascularization of the parathyroid from thyroid, laryngeal, and pharyngeal branches as demonstrated by G. Curtis do not need surgical attention after the main ligature. The wound is closed tight or with drainage as one prefers in goiter work.

In the after-care we have given as a routine 20 units of parathormone daily for a week after the operation. Blood calcium is determined every day or two. If it sinks below 7, the parathormonal dose is increased and calcium gluconate is given intravenously. If tetanic symptoms occur, obviously enough should be given to control the symptoms. Blood calcium provides a good index as to the need and discontinuance of parathormone and calcium.

It seems that postoperative tetany is not more to be feared after parathyroidectomy in parathyroidism than myxœdema after the operation for Grave's disease. The handling of the recurrent nerve in one of our 18 operations, caused dyspnœa on the operating table. A tracheotomy tube left for 24 hours gave prompt relief without any lasting damage.

Addenda.—In *The British Journal of Surgery*, vol. xix, No. 74, October 1931, page 285, Dr. A. James Walton of the London Hospital, London, England, in my opinion gives a rather important contribution to the technique of parathyroidectomy. He especially mentions that tumors have been overlooked on account of their location behind the thyroid fascia. Such location of the parathyroid, while not frequent, seems to occur and a tumor was overlooked in one of Donald Hunter's cases by Walton and was found at a second operation by splitting the thyroid fascia. This position of a parathyroid tumor should, therefore, be kept in mind in case it is not found in the usual place right back of the thyroid body.

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TUMORS OF THE MESENTERY

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TUMORS which originate within the leaves of the mesentery, because of their exceedingly uncommon occurrence, are looked on as unique surgical lesions. Nevertheless, even a cursory search of the literature reveals several hundred cases which have been observed, diagnosed, and reported.

In the files of The Mayo Clinic are records of 22 cases which we have reviewed and summarized, and now offer as additions to the literature on this subject. The bizarre clinical picture which most of these tumors present, the surgical difficulties which attend their extirpation, and their pathological identification are of no more interest than their development. The etiological factors concerned in the production of these tumors remain largely conjectural but, unquestionably, a certain number of them depend on congenital defects in the development of the mesentery for their explanation.

The embryology of the mesentery and its morphological relationship to neighboring structures is of unquestioned significance in the production of certain types, and probably of the majority, of these tumors. The primitive alimentary canal is developed within the cavity of the cœlom, within the median partition which separates the right cœlomic space from the left. This median partition suspends the primitive gut to the dorsal body wall and forms the dorsal mesentery, whereas that part of the partition which fixes the digestive tract to the ventral body wall constitutes the primitive ventral mesentery. However, the latter is formed only in connection with the foregut and the cloacal segment of the hindgut; all the remainder of the digestive tract is destitute of ventral mesentery. In the adult, the ventral mesentery is represented by the gastrohepatic omentum and the falciform ligament.

The fate of the dorsal mesentery is more complex than that of the ventral. Early in development, the cœlom extends into the proximal segment of the umbilical cord, and it is within the umbilical recess of the peritoneal cavity that the midgut undergoes its earliest developmental changes. This U-shaped loop of gut is made up of a proximal jejunal and a distal, or cæcal, limb. As rotation of the digestive tract takes place the jejunal limb comes to lie to the right and dorsal to the cæcal part. The mesoduodenum becomes adherent to the body wall, and about the tenth week of fetal life the umbilical loop of gut is retracted within the peritoneal cavity.

As the superior mesenteric artery descends to the intestinal loop, it gives off three branches to the posterior limb; these are the middle colic, right colic, and ileocolic arteries. The mesentery of the U-shaped loop is divided into two parts by this vessel. The pre-arterial part gives rise to the greater part of the mesentery of the small bowel, whereas the mesentery of the posterior limb, or postarterial part, is destined to form the mesentery of the ascending and transverse colon, and also the lower part of the mesentery of the small bowel.

When the rotation of the intestinal loop occurs, the splenic flexure of the colon comes against the spleen, while the transverse mesocolon comes into contact with that part of the mesogastrium which forms the great omentum and completes the formation of the transverse mesocolon. As is well known, the ascending and descending parts of the colon lose their mesentery after rotation has been completed, and become adherent to the dorsal body wall.

From an embryologic standpoint, it is conceivable that remnants of the wolffian or muellerian ducts, or segregated remnants of the genital gland can become lodged within the mesentery. The genital ridge develops lateral to the mesentery of the gut. The genital and the wolffian bodies each has its own mesentery, but these mesenteries have a common attachment—the common urogenital mesentery. The duct of the wolffian body is situated in the lateral margin of the genital ridge, dorsal to the muellerian duct. It is possible that portions of these embryonic structures might migrate in the retroperitoneal tissues to invade the mesentery of the bowel, and act as nuclei of mesenteric tumors in postnatal life.

Mesenteric neoplasms were recognized as early as the sixteenth century, when Benivieni, a Florentine anatomist, described the first cyst to be

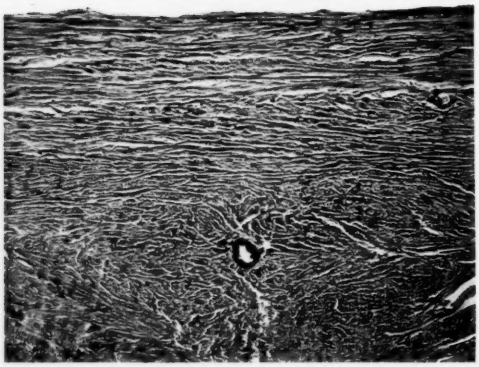

Fig. 1. Wall of serous cyst. Case 1.

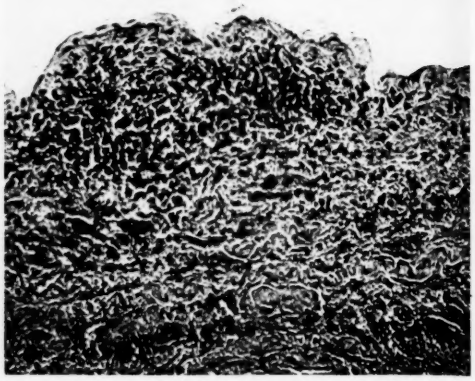

Fig. 2. Wall of serous cyst. Case 5.

reported in that structure. Nevertheless, little significance was attributed to these tumors until the middle of the last century. In 1880, Tillaux first successfully removed a mesenteric tumor, and this undoubtedly did much to stimulate interest in the subject. Only since 1897 has careful study of these growths been made.

Due to our lack of knowledge concerning the pathogenesis of the various types of mesenteric tumor, the classifications are necessarily at variance. In 1803, Portal (15) grouped these neoplasms as scirrhous, steatomatous, stony, cancerous, and hydatid. Moynihan introduced the following classification for mesenteric cysts: serous, chylous, hydatid, sanguineous, dermoid, and cystic malignant disease or cystic sarcoma. Dowd employed a more inclusive grouping which was: embryonic cysts, hydatid cysts, and cystic malignant disease. Ewing (8) designated the tumors as chylous, enteric, and dermoid cysts and intraperitoneal cysts of nephrogenic origin. Rawls included the following tumors among the solid neoplasms of the mesentery: lipoma, fibroma, carcinoma, and sarcoma.

In 1897, Moynihan estimated that 100 cases of mesenteric cyst had been reported prior to that time, whereas Harris and Herzog during the same year collected 57 cases of the solid type of tumor. In 1900, Dowd reviewed 145 cases of mesenteric cyst from the literature. In 1909, Deaver found 39 additional cases. In 1924, Rawls stated that approximately 200 cases of cystic tumor of the mesentery had been reported; in 1926, Clark put the number at 300; in 1930, Joyce, Howard, and Fitzgibbon estimated that between 200 and 300 cases had been described.

It is the consensus of opinion that cystic tumors of the mesentery are more prevalent than the solid variety, as has been stated by Jones and McClure, and by Munro.

Mesenteric cysts of the chylous variety are more common than any other cystic neoplasm of that structure. Of the solid tumors, the lipomata are said to be the most common, whereas Bowers has stated that the fibromata are the most uncommon of the solid mesenteric tumors. Moynihan showed that multilocular cysts of the mesentery are more often encountered than those of the unilocular type, and furthermore that unilocular cysts are more common in the mesocolon than in the mesentery. The same author has stated that cystic mesenteric disease is much more common in women than in men, whereas the hæmorrhagic type of cyst is found with about the same frequency in the two sexes. On the contrary, Joyce, Howard, and Fitzgibbon expressed the belief that the incidence of mesenteric cysts is about equal in males and females.

These cysts may occur in any part of the mesentery. Deaver thought that the neoplasms are most common near the termination of the ileum, and are found less frequently in the mesentery of the jejunum, cæcum, and mesocolon.

Joyce, Howard, and Fitzgibbon found mesenteric cystic disease to be most prevalent in the decade of life between 30 and 40 years.

The origin of mesenteric cysts has been a matter of conjecture since the tumors were first described. Dowd reviewed the anatomy of the primitive genito-urinary organs and the alimentary canal, and postulated as to how readily a sequestration from the embryonic genital gland

Fig. 3. Wall of hæmorrhagic cyst. Case 6.

Fig. 4. Hæmorrhagic cyst showing adherent section of intestine. Case 7.

could be included within the folds of the mesentery, mesocolon, or mesorectum. He considered serous cysts to be of embryonic origin, whereas sanguineous cysts owed their nature to a hæmorrhage occurring into a preformed cyst. Carter was also of the opinion that many, if not all, of these cysts are of embryonic origin. He thought that they might arise from a Meckel's diverticulum, or from sequestration from the bowel during development, although obstruction of the lymphatic channels probably results in cysts in certain cases. Moynihan, on the contrary, sponsored the view that mesenteric cysts are of multiple origin. He thought that the serous type may have a two fold origin: from a dilatation of a portion of a lymphatic vessel, occluded probably as the result of some inflammatory condition, or from a hæmorrhage between the layers of the mesentery. He considered the usual etiological factor in the formation of hæmorrhagic cysts to be trauma. Hæmorrhage into the mesentery may result in several alternatives, he postulated: a large hæmorrhage may develop into a cyst, the hæmorrhage may occur into a pre-existing cyst, or into a solid tumor of the mesentery, the greater part of the solid constituents of the effused blood may disappear and a simple serous cyst result, or, finally, the fluid component of the blood may be absorbed and a more or less solid tumor persist. He further hypothesized that dermoid cysts may arise not only from remnants of ovarian tissue, but from the remains of the wolffian, muellerian, or vitelline ducts, the latter in connection with a Meckel's diverticulum. Porter subscribed to Moynihan's views in regard to the multiple origin of mesenteric cysts. Royster advanced the theory that sanguineous cysts of the mesentery may be due to embolism or thrombosis of its vessels.

The pathogenesis of chylous cysts of the mesentery has been the subject of a long controversy. Rokitansky was of the opinion that these cysts had their origin in degenerated lymph nodes, and his contemporary, Virchow, concurred with that view. Moynihan thought that possibly the underlying pathology of these cysts is a dilatation of the lacteals of the mesentery that is an exaggerated condition of lymphatic varix. Ewing (9) has stated that the chyle-angioma of the mesentery is a cavernous lymphangioma containing milky fluid which arises from congenital or from acquired obstruction of the lymph vessels. Spaeth thought that chylous cysts could be produced by stasis in the lymph passages coincident with formation of infarct, the infarcts being made up of dried masses of chyle, with a concomitant degeneration of the lymph nodes belonging to the system. In support of this view is the occasional finding of lymph nodes within the walls of these cysts. Dowd and Westman thought the foregoing theory untenable because of the rich anastomosis between the vessels of the lymphatic bed. Dowd was of the opinion that the chylous nature of the cyst is due to effusion of chyle into a preexisting cyst. Wilson conceded that the latter view may be correct in certain cases, but he contended that the cyst may be primarily chylous in certain other cases. Crane regarded these tumors as true lymphangio-lymphomata.

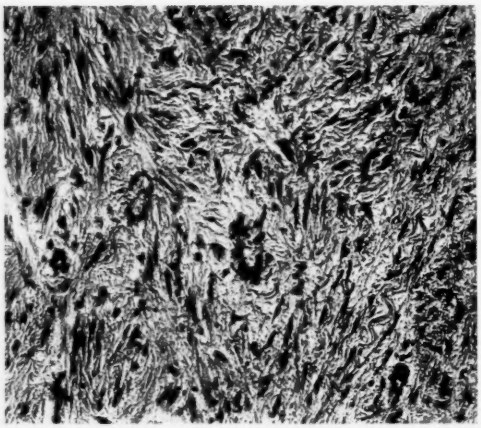

Fig. 5. Fibromyoma. Case 13.

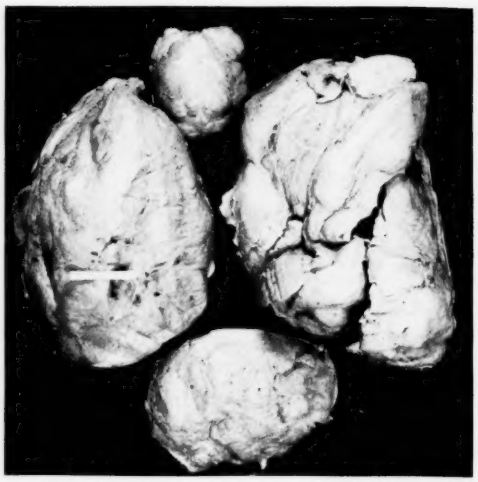

Fig. 6. Fibromyxoma. Case 14.

The diagnosis of mesenteric tumors is difficult because of the multiplicity of symptoms produced by these growths. Moynihan has stated that the most characteristic signs of mesenteric cyst are: (1) prominence of the fluctuating tumor toward the umbilicus; (2) great mobility, especially in the transverse direction, and sometimes about a central axis; and (3) presence of a zone of resonance around, and a belt of resonance across, the cyst. These are three diagnostic signs of Tillaux.

Little need be said of prognosis in regard to mesenteric tumors. Benign cystic growths can be removed with only slight mortality, whereas malignant tumors here, as elsewhere, give a poor prognosis.

The cases presented in this paper are all instances of primary tumor of the mesentery; those arising secondary to a growth elsewhere, and neoplasms definitely arising in the lymph glands have been excluded. In the present series the cystic tumors occurred less frequently than the solid variety in the proportion of 7 to 15.

SEROUS CYSTS

Two cases of serous cyst are included in the present series. In neither case was a lining membrane demonstrable in the wall of the cyst, although multiple sections were made of both tumors.

Case 1. A woman, aged 46 years, had experienced generalized, intermittent, cramp-like abdominal pain during the year prior to operation; the pain was not definitely related to meals. During the year she had lost 25 pounds (11.3 kilograms) in weight. Roentgenologic examination revealed the presence of a duodenal ulcer, but it did not seem probable that this lesion was responsible for the generalized abdominal symptoms. At operation the pelvic organs were found to be normal in appearance, but a cystic mass measuring 12 by 5 centimeters was found in the mesentery of the sigmoid. The wall of the cyst was composed of rather dense connective tissue, and there was practically no inflammatory reaction. A definite lining membrane could not be demonstrated. (Fig. 1.)

Case 2. A man, aged 34 years, noticed a mass in the lower left abdominal quadrant 1 month previous to his coming to the clinic. The only other pertinent point in the history was the complaint of dull, gnawing, epigastric distress, without relationship to the taking of food, of the same duration as the mass. Roentgenologic examination of the stomach and duodenum gave negative results. On exploration, a cyst, 7 or 8 centimeters in diameter, was found in the mesentery of the sigmoid. The microscopic picture presented by this tumor was similar to that of Case 1; the wall was composed of connective tissue, and there was no demonstrable lining membrane.

CHYLOUS CYSTS

The chylous cysts in the present series differed from the serous variety in two important respects: whereas the serous tumors did not possess an epithelial or endothelial lining, those of the chylous type had an endothelial lining; furthermore, all three of the chylous cysts occurred in the mesentery of the small intestine; this was not true of the serous neoplasms. Definite lymph follicles could not be demonstrated in the walls of the cysts in any of these cases, although there were many irregular accumulations of lymphocytes.

Case 3. A man, aged 24 years, 3 weeks prior to operation had palpated a mass in the lower part of the abdomen, but had not experienced pain. Obstinate constipation was the only other complaint. At operation a cystic mass was

Fig. 7. Sarcoma with resected loop of intestine. Case 15.

found in the mesentery of the small intestine, 4 feet (120 centimeters) from the origin of the jejunum, which contained 8 ounces (240 cubic centimeters) of milky fluid. The dilated lacteals were visible grossly. The wall of the cyst was made up of dense connective tissue, with many collections of lymphocytes. A distinct endothelial lining membrane was demonstrable.

CASE 4. A woman, aged 42 years, noticed a mass in the lower part of the abdomen 5 years before coming to the clinic, but there were no associated symptoms except an occasional attack of severe lower abdominal pain which was precipitated by turning about suddenly. At operation a cystic tumor of the mesentery of the upper part of the ileum was found, which was adherent to the anterior abdominal wall, as well as to several loops of the small intestine, although there was no obstruction of the bowel. The microscopic picture of the tumor was similar to that of Case 1 except that the wall of the cyst was more cellular and contained less fibrous connective tissue.

CASE 5. A man, aged 62 years, gave a history of having had discomfort in the right lower quadrant of the abdomen for 2 years. It came on after meals, amounting only to a feeling of fullness. A mobile tumor, 7 or 8 centimeters in diameter, was easily palpable. The tumor was found to arise in the mesentery of the small intestine, opposite a Meckel's diverticulum, and was easily enucleated without seriously impairing the blood supply of the intestine. The mass measured 9 by 9 by 7 centimeters and contained a milky fluid. The wall of the cyst was composed of dense connective tissue, with many scattered collections of lymphocytes. Here, also, the wall of the cyst was lined with endothelium (Fig. 2).

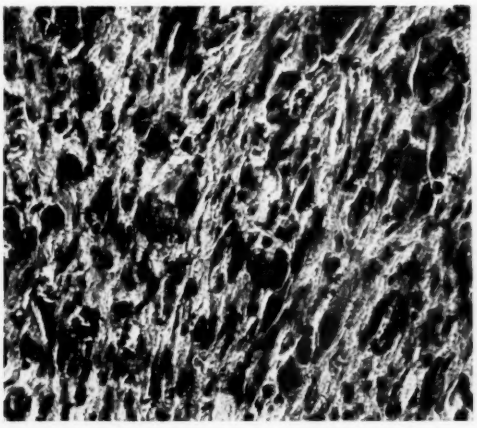

Fig. 8. Sarcoma showing several mitotic figures. Case 15.

SANGUINEOUS CYSTS

The source of the blood in this type of cyst is a matter of conjecture. In neither of the cases of this series was a history of trauma elicited, nor was any co-existing condition found which could have been responsible for the hæmorrhage into the mesentery.

CASE 6. A woman, aged 39 years, had complained of intermittent, gnawing, epigastric pain during the 2 years prior to coming to the clinic. The pain was not related to meals. At operation a cyst of the mesentery of the small intestine was found; it was 7 or 8 centimeters in diameter, and rested on the superior mesenteric vessels. The cyst was filled with dark blood. The wall was composed of fibrous tissue, with considerable chronic inflammatory exudate, and without a demonstrable lining membrane. A moderate amount of blood pigment was present (Fig. 3).

CASE 7. A girl, aged 6 years, had experienced recurrent attacks of vomiting during the 5 years previous to operation. The attacks had come on every 3 to 4 months, with frequent vomiting for a period of 2 to 7 days. Intense pain in the lower part of the abdomen and bloody stools were associated with the attacks, and constipation was also a marked symptom. At operation a lobulated tumor, about 8 centimeters by 12 centimeters in different diameters was found in the mesentery of the ileum; the tumor was cystic and contained dark red fluid. The intestine above the mass was dilated, and removal of the cyst necessitated resection of a loop of the intestine. The wall of the cyst was similar to that of the former case, and here again no lining membrane could be detected (Fig. 4).

LIPOMATA

Lipomata are relatively common in the mesentery, and it seems highly probable that small, fatty tumors occur more often than is generally supposed. Fatty tags, and even larger accumulations of fat, frequently are found in the mesentery in the course of abdominal operations.

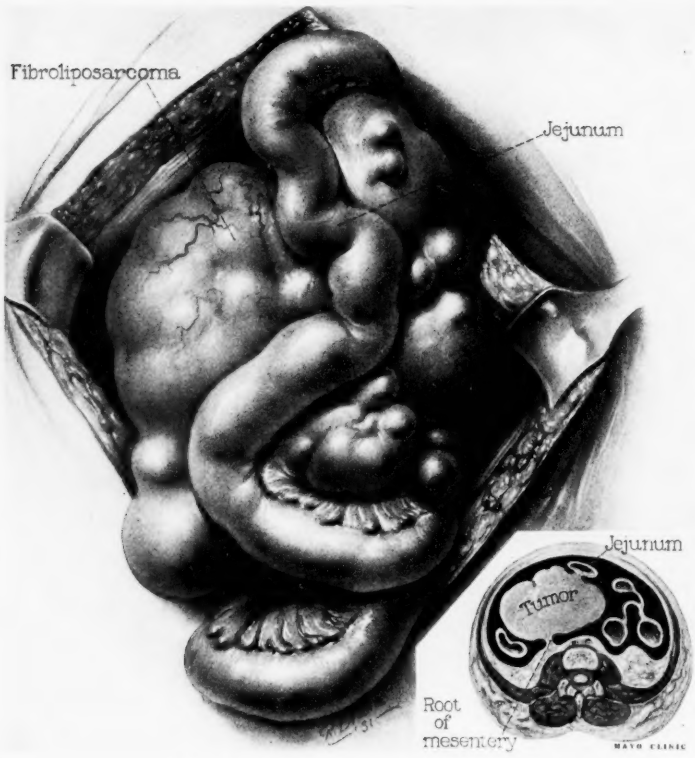

Fig. 9. Fibroliposarcoma of the jejunum.

CASE 8. A woman, aged 57 years, had complained of distress in the lower part of the abdomen during the 2 months prior to coming to the clinic. A movable epigastric mass 7 or 8 centimeters in diameter, was readily palpable. At operation the mass proved to be a lipoma which was situated about 6 feet (180 centimeters) from the duodenojejunal juncture.

CASE 9. A woman, aged 28 years, noticed a mass in the lower part of the abdomen 6 months previous to operation. She had also experienced pain in the lower part of the abdomen, which she described as menstrual in type. There was an associated carcinoma of the cervix. At operation a degenerated lipoma was removed from the mesentery of the small intestine.

CASE 10. A man, aged 38 years, gave a history of dull, lower abdominal pain of 2 months' duration. A large, fatty tumor of the mesentery of the sigmoid was found, which completely filled the pelvis. The patient also suffered from chronic ulcerative colitis.

CASE 11. A man, aged 46 years, had complained of pain in the upper part of the abdomen for several years. He had palpated an epigastric mass about 2 months before coming to the clinic. Multiple fatty tumors of the mesentery of the small intestine were found; the largest was about 8 centimeters in diameter.

CASE 12. A woman, aged 46 years, had experienced increasing constipation over an interval of 6 months. An indefinite epigastric mass was palpable. At operation, a fatty tumor 7 or 8 centimeters in diameter was removed from the mesentery of the upper part of the jejunum.

FIBROMATA

These neoplasms are of interest chiefly because of their rarity, and because of the fact that they are prone to be confused with malignant growths of the mesentery. Two cases are included in the present series, one of fibromyoma and the other of fibromyxoma.

CASE 13. A woman, aged 25 years, had been conscious of a mass in the lower right abdominal quadrant 18 months before coming to the clinic. During this period she had complained of a dull, intermittent pain in the same region. Constipation had alternated with diarrhœa, and on one occasion she had noted tarry stools for a week. Urinary frequency was also a pronounced feature of her history. At operation, an encapsulated tumor measuring 11 by 8 by 7 centimeters was found in the mesentery of the lower part of the ileum, and 15 inches (38 centimeters) of the terminal ileum were resected in the course of removal of the tumor. The pelvic organs were normal in appearance. Microscopically the tumor was found to be composed of

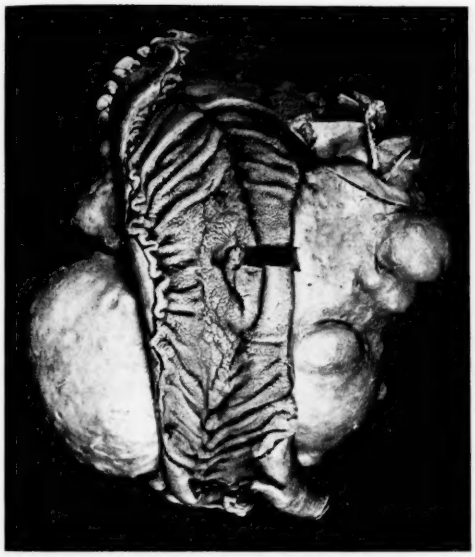

Fig. 10. Sarcoma showing adherent section of intestine. Case 20.

smooth muscle cells, with a liberal amount of connective tissue stroma (Fig. 5).

CASE 14. A man, aged 50 years, had experienced a sensation of epigastric fullness over a period of 10 years; the pain was aggravated by the taking of food. The only other pertinent symptom was increasing constipation. A large mass was felt in the lower right abdominal quadrant, and the superficial veins of the abdominal wall were enormously dilated. At operation a large tumor was removed from the mesentery of the small intestine. The growth measured 45 by 40 by 25 centimeters and weighed 25 pounds. It was composed largely of myxomatous tissue, with a considerable amount of fibrous connective tissue stroma. The tumor had undergone moderate necrosis in places (Fig. 6).

MALIGNANT TUMORS

As already has been stated, all secondary tumors of the mesentery have been excluded from consideration. The number of cases of sarcoma exceeded that of any other single group of cases in the present series.

CASE 15. A man, aged 45 years, came to the clinic with a history of intermittent, cramp-like pain across the lower part of the abdomen, of 4 months' duration. More recently he had had night sweats, and a daily elevation of temperature. He had lost 26 pounds (11.8 kilograms) in weight. Examination of the blood disclosed nothing of importance except mild secondary anæmia, and a leucocyte count ranging from 23,300 to 33,000 cells in each cubic millimeter of blood. A large abdominal mass was palpable, and extended from the costal margin to the umbilicus. Laparotomy revealed a large, sausage-shaped tumor, the upper end lying over the spleen, and the lower end over the ileocæcal region. The neoplasm had its origin in the mesentery

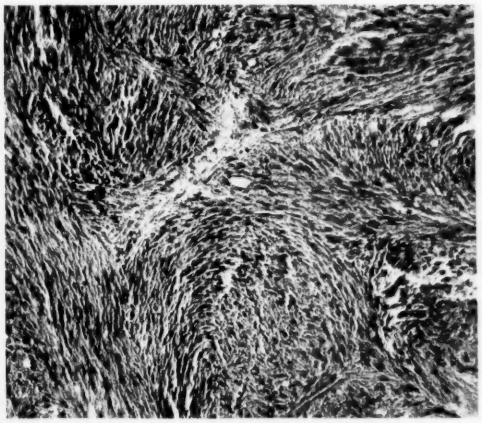

Fig. 11. Sarcoma. Case 20.

of the small intestine, close to the duodenojejunal juncture and extended into the mesentery for a distance of 12 to 18 inches (30 to 45 centimeters). There was slight thickening of the musculature of the bowel, but no gross obstruction. The growth was removed, together with 45 centimeters of the ileum, an end-to-end anastomosis was done over a clamp, and a Witzel enterostomy was done 10 inches (25 centimeters) below the point of anastomosis. The patient recovered. The tumor was found to be necrotic in places and was composed of fibrous connective tissue, with numerous regions of myxomatous tissue. Numerous mitotic figures were present, and the tumor was malignant in appearance. The pathologists diagnosed the tumor a fibroliposarcoma (Figs. 7, 8, and 9).

CASE 16. A woman, aged 68 years, complained of dull distress in the lower left abdominal quadrant, of 3 years' duration, with an occasional cramp-like pain in this region. She had lost 20 pounds (9 kilograms) in weight. At operation, a mass, about 10 by 12 centimeters was removed from the mesentery of the small intestine through an opening in the gastrohepatic omentum. Microscopically, the tumor was found to be a fibromyosarcoma of a low grade of malignancy.

CASE 17. A man, aged 54 years, came to the clinic with a history of periodic attacks of epigastric distress of 6 weeks' duration. The pain was aggravated by the taking of food, and alkalies afforded him only slight relief. He had lost 15 pounds (6.8 kilograms) in weight in the course of his illness. An inoperable fibrosarcoma of the mesentery of the small intestine was found, and a palliative intestinal anastomosis was done.

CASE 18. A man, aged 44 years, complained of pain in the epigastrium in the lower left abdominal quadrant of 8 months' duration. Occult blood had been found in the stools 2 months prior to his coming to the clinic. Examination of the blood revealed marked secondary anæmia. A cystic mass was found in the mesentery of the small intestine, arising 2 inches (5 centimeters) from the origin of the jejunum. The wall of the cyst was very vascular, and material aspirated from the tumor had a fæcal odor, due to perforation of the intestine by the growth. The neoplasm proved to be a fibrosarcoma.

CASE 19. A man, aged 40 years, gave a history of shooting pain in the lower part of the abdomen of 18 months' duration. Except for increasing constipation, and loss of

weight of 25 pounds (11.3 kilograms) there was nothing else of importance in the history. At operation a tumor about 10 centimeters in diameter was found to arise 2 feet (60 centimeters) from the origin of the jejunum; the growth was in close relation to the superior mesenteric vessels. Microscopically the tumor was found to be composed chiefly of myxomatous tissue with a relatively small amount of fibrous tissue. The grade of malignancy was low.

CASE 20. A man, aged 53 years, complained of general loss of strength, constipation, bloody stools, and lower abdominal soreness of 1 year's duration. Two months prior to his coming to the clinic a mass had been palpated in the lower part of the abdomen. At operation, a tumor about 12 centimeters in size was removed from the mesentery of the ileum, together with 27 centimeters of intestine. Microscopically, the mass was found to be made up of spindle-shaped cells, arranged in a very irregular manner. There was marked variation in the size of the nuclei, with many mitotic figures. The patient returned to the clinic 6 years after the primary operation, with metastatic involvement of the liver (Figs. 10 and 11).

CASE 21. A man, aged 56 years, stated that he had experienced dull lower abdominal pain and three attacks of colic over a period of 5 years. Signs of peritonitis developed, and emergency laparotomy was done. Multiple cysts of the mesentery of the small intestine were found, the largest of which was about 10 centimeters in diameter. The latter cyst was necrotic in appearance and had ruptured, causing the peritonitis. The cyst wall was found to be sarcomatous in character. He died 6 days after exploration.

CASE 22. A man, aged 60 years, complained of increasing constipation over an interval of 2 years. In the 2 months prior to operation he had lost 15 pounds (6.8 kilograms) in weight. No other symptoms were elicited. A large tumor was found, which was adherent to both the mesocolon and to the mesentery of the small intestine, and the wall of the duodenum was somewhat eroded by the growth. Microscopically the tumor was found to be a very malignant myxosarcoma.

SUMMARY

Twenty-two cases of primary tumor of the mesentery have been reviewed briefly. From an embryological point of view it is conceivable that mesenteric tumors may arise from displaced remnants of the genital gland, wolffian body or its duct, or from the muellerian duct. Nevertheless, there is no proof that any of the tumors described here owed their pathogenesis to such embryonic remains. Our data contribute nothing to the origin of serous cysts, but due to the fact that an epithelial lining was not demonstrable in these tumors, it is conceivable that they may have had their origin in hæmorrhage into the mesentery, the solid constituents of the blood having been absorbed. The endothelial lining of the chylous cysts favors the view that these neoplasms are due to dilatation of the lymph spaces, rather than being due to effusion of chylous material into a preformed cyst. The sanguineous cysts would appear to be due to effusion of blood into the mesentery, and do not seem to be hæmangiomatous. The pathogenesis of the lipomata and sarcomata is easier to understand than that of the cystic tumors.

In this series the solid neoplasms occurred more frequently than the cystic variety, and sarcoma constituted the largest single group of the series. The tumors showed no definite predilection for either sex.

The chylous cysts all occurred in the mesentery of the small intestine, whereas such was not necessarily the case with the other types of cyst.

The prognosis of the benign tumors is favorable in spite of a pessimistic note having been struck in the literature on this point. In cases of malignant tumor the outlook is unfavorable.

The diagnosis of mesenteric neoplasms is difficult, but given a mobile abdominal mass extrinsic to the gastro-intestinal tract, the possibility of mesenteric neoplasm should be borne in mind. The occurrence of these tumors is probably much more common than has been believed.

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NEPHROSTOMY: INDICATIONS AND TECHNIQUE[1]

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THE operation of nephrostomy, more or less formally done, has been in common use for more than 40 years. During the earlier period it was usually applied to much overdistended kidneys and was usually an emergency measure carried out without the possibility of any very complete knowledge of the condition of the upper part of the urinary tract. On the other hand, as early as 1898 there was a pretty full discussion of this subject by Guyon and Albarran. They drew attention to the apparently great ability of renal tissue to resist infection if it was not already present, and to shake off infection if it had occurred provided, always, satisfactory drainage of the kidney by nephrostomy was achieved. They noted the ability of the kidney again to take up its function "to an extent more or less complete according to the damage which has been produced. If the obstruction has been of short duration, function is but little disturbed. If the retention has been of long duration, it will have produced a more or less irreparable damage to the parenchyma and renal function is to that extent, permanently damaged."

Much of the literature concerns itself with questions of technique which have, of course, been much modified during the period elapsed. Pakowski, in 1913, presented an extensive discussion of this subject including a considerable investigation of the return of renal function and of the ability of the kidney to resist or rid itself of infection. He stated his agreement with the principles laid down by Albarran in 1898.

There thus appear to be two very important principles involved: one, the ability of the kidney to deal with infection, and the other the effect on renal function. Writers, particularly of the French school, stress the ability of the kidney to deal with infection. On the other hand, other writers, particularly Joly, regard infection as a very serious matter, and Joly points out that in his experience infection of the kidney with urea-splitting organisms, particularly staphylococci and the proteus, gives a very unfavorable prognosis. He expressed the opinion that infection of one kidney with these organisms is very likely to be transmitted to the other kidney through the blood stream, and said: "Once a bilateral infection is firmly established, the outlook is very bad, and the patient usually dies of uræmia. The process is necessarily slow, but it is none the less sure." This observation leads him to advise nephrectomy when such an infection has occurred in order to avoid involvement of the other side. These two sets of views are so much at variance that it seems desirable to attempt a collection of evidence which will determine which, if either, is to be regarded as basic.

The early observers were impressed by the rapid return of function among patients with high grade renal obstruction treated by this method. On the other hand, Hinman, in 1922 and subsequently, did some very important work on the problem of repair after obstruction and laid down the principles of what he termed renal counterbalance. These observations are obviously of very fundamental importance and, if we accept fully his thesis that, in the presence of hypertrophy of the kidney on the other side, an obstructed kidney is likely to go on to complete atrophy, many of the situations likely to appear favorable for nephrostomy should, in fact, be treated by nephrectomy. It is, of course, difficult to apply his doctrine to the cases which we see clinically because the situation is rarely if ever quite so clean-cut as in experimental work. That

[1]Read before the American Association of Genito-Urinary Surgeons, Buck Hill Falls, Pennsylvania, June 4 to 6, 1931.

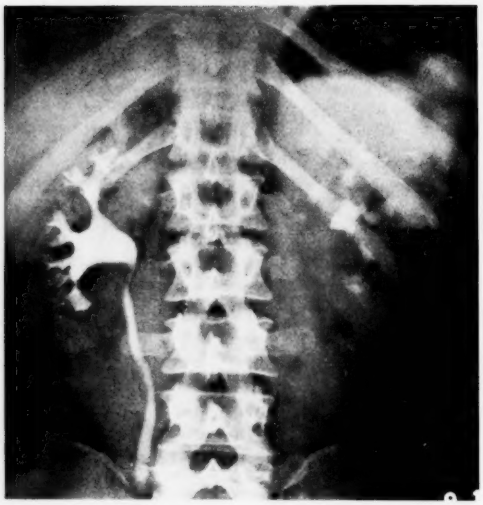

Fig. 1. A man aged 28 years with calculous pyonephrosis on left side and pyelogram of right kidney showing stone in lower calix.

his conclusions may not be quite so far-reaching is suggested by the work of Joelson, Beck, and Moritz, published in 1929, in which they went over the ground covered by Hinman and were unable to agree with his conclusions. They say quite dogmatically: "Our experiments did not

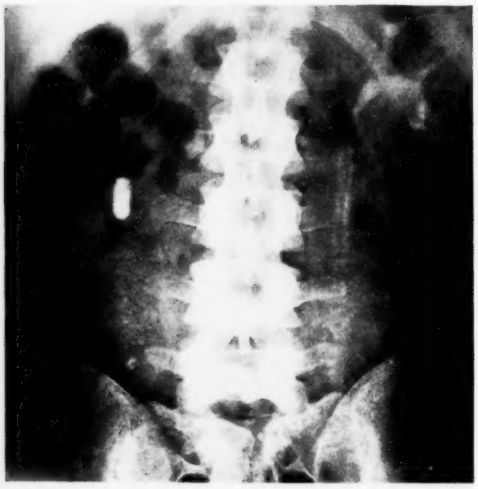

Fig. 3. A man aged 28 years 15 minutes after injection of skiodan. The absence of evidence of renal function on the right side may be noted.

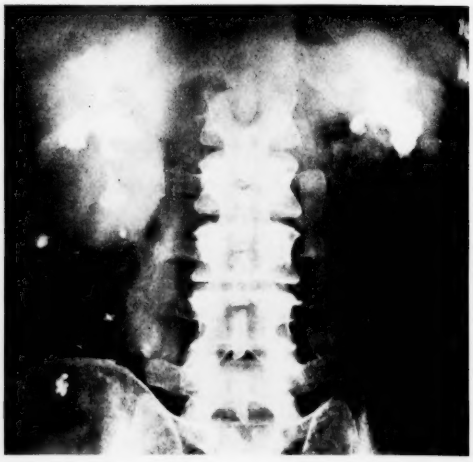

Fig. 2. Bilateral calculous pyonephrosis in a man aged 51 years. Right nephrostomy was done followed by rapid improvement of renal function.

demonstrate any renal atrophy of disuse and in fact strongly suggest that such atrophy does not occur. In view of the experimental data presented the theory of renal counterbalance need not be seriously considered in deciding the surgical treatment for certain renal lesions." This evidence of disagreement between capable experimenters may be taken to authorize us at least to reserve our judgment as to the extent to which atrophy will occur where the injured kidney is working in competition with an hypertrophied kidney on the other side. As already pointed out, the clinical situations are by no means as clean-cut as those produced by experimental surgery, and consequently the field of application of Hinman's doctrine may be considerably limited. We think we are at least authorized to regard the doctrine as a not very important factor to be considered in the clinical application of nephrostomy, and we should be on sound ground by using the operation perhaps more widely than has been the habit in the past, partly at least for the purpose of establishing clinical results and forming the basis for an opinion of the weight to be given by the quite opposite opinions held by such observers as Pakowski and Joly.

INDICATIONS

In general terms, the indications for nephrostomy are the presence of obstruction which cannot be satisfactorily remedied by some other method. There is also perhaps a satisfactory indication in preventing progressive injury to kid-

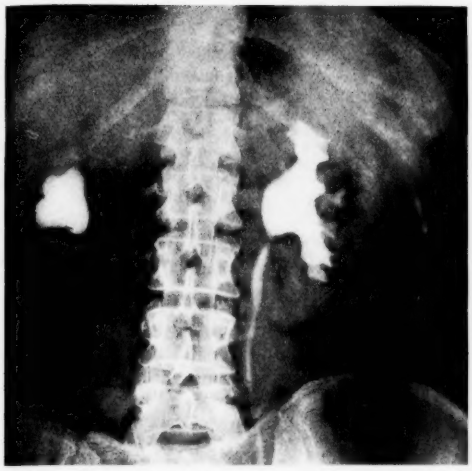

Fig. 4. A woman aged 55 years. Right calculous pyonephrosis.

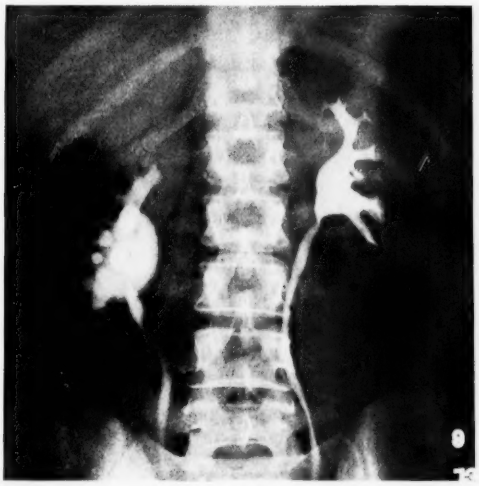

Fig. 5. A woman aged 51 years. Bilateral pyelogram showing right infected hydronephrosis, successfully treated by plastic operation on pelvis and temporary nephrostomy.

neys in which there is incomplete obstruction which favors the continuance of infection as for instance in patients with bilateral calculous disease with steadily waning renal function. Another group with somewhat similar implications are those with inflammatory lesions perhaps primary in the bladder, but which have invaded the upper part of the urinary tract and in which drainage of the kidney is thus seriously and more or less permanently interfered with. Here also may be considered that group of patients with as yet unexplained lesions apparently of the nerve supply resulting in abnormal vesical function with dilated ureters and renal pelves. In both of these groups of cases renal function is apparently being slowly but steadily destroyed and will go on to the stage of renal insufficiency unless its progress is halted. If it is true that nephrostomy can be done without danger of progressive renal infection and if it is true that by nephrostomy renal function can be improved or maintained over a period of years, there develops here a relatively clear indication. In general one may consider the application of nephrostomy to the following conditions:

1. Acute obstruction of both ureters or of remaining one as in calculous anuria or malignant disease constricting the lower end of the ureter.

2. Hydronephrosis or infected hydronephrosis in which the cause of the obstruction may be removable, but in which drainage of the kidney as a temporary measure is indicated to improve function. In this group of cases there may develop some in which the nephrostomy may have to be permanent.

3. Renal calculi. There are here at least two distinct groups for which nephrostomy temporary or permanent may be desirable. In one group are cases in which there is considerable destruction from high grade blocking of the outlet but in which the removal of stone will substantially relieve the difficulty. For some of these cases at least temporary nephrostomy may be desirable for the purpose of permitting readjustment be-

Fig. 6. A man aged 34 years. Right nephrostomy has been done and straight tube is in position. Calculi in left kidney may be noted.

Fig. 7. Marion's method of nephrostomy.

tween the pelvis and the ureter, to allow rapid recovery of renal function, and, at least possibly, to aid in the quieting of renal infection.

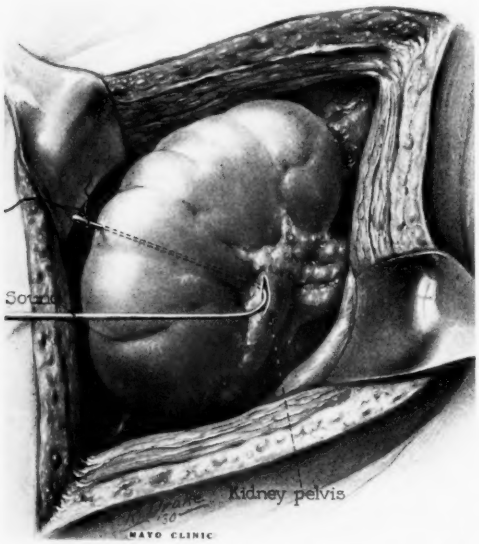

Fig. 9. Method of introducing uterine sound into pelvis, passing it out through renal cortex and attachment of silk guide.

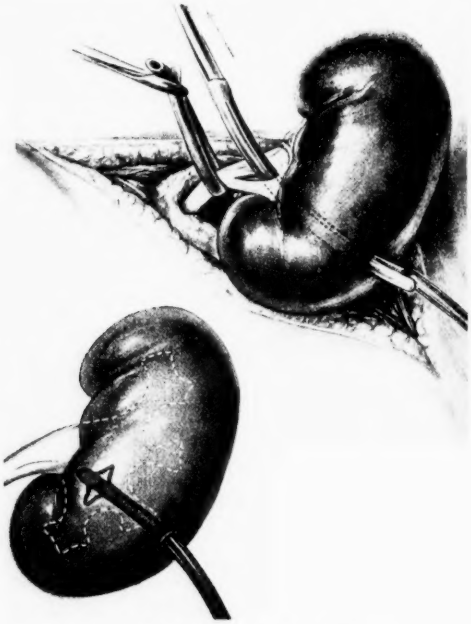

Fig. 8. Papin's method of nephrostomy.

Another group includes cases of bilateral stone formation of the type which is not now regarded as satisfactory for treatment by removal of the stones. There is a considerable number of these in which massive stone formation occurs on both sides with relatively few symptoms but after a time leads to progressive failure of renal function which will prove fatal if it cannot be relieved. It will be remembered that Watson, in 1910, suggested nephrostomy for relief of some of these patients, and on at least one patient he performed bilateral nephrostomy, which maintained satisfactory renal function for more than 10 years. In this connection we would suggest that there appears to us to be some possibility that nephrostomy maintained for a considerable period may have a very definite influence on the formation of stone, although we do not think that the evidence on this point will as yet warrant any conclusion. A recent publication by Boyd calls attention to this point and at least in one of Watson's cases stones appeared to develop with much less rapidity after nephrostomy. We think, therefore, that in this group it may appear that there is more than one ground on which nephrostomy, permanent or semi-permanent, may be advised.

4. Nephrostomy must, perhaps at least for the

present, be retained as an occasional method of diverting the urinary stream in carcinoma of the bladder thought suitable for total cystectomy.

5. We would here include that obscure group of cases in which the failure of the muscular apparatus of pelvis, ureters, and bladder satisfactorily to evacuate the urine leads to progressive atrophy of the kidneys. This group will doubtless become increasingly amenable to treatment by other methods, but we are at present faced with a certain number of these patients in whom renal insufficiency threatens, relief cannot be assured by other methods, and nephrostomy may be relied upon to check further damage and perhaps allow for some measure of regeneration.

6. We would here include a group of cases of renal infection without high grade obstruction in which the nephrostomy is done as a method of avoiding recurrent renal infection and allowing some amount of renal recovery.

TEMPORARY OR PERMANENT NEPHROSTOMY

The decision as to whether nephrostomy should be temporary or permanent will not ordinarily be difficult. Permanent nephrostomy should probably be reserved for those cases in which the condition for which nephrostomy is done cannot be remedied or at least cannot be remedied to a permanently satisfactory extent. In a few cases nephrostomy which has been maintained as a temporary measure will have to be made permanent since methods to relieve the obstruction have failed. The duration of temporary nephrostomy will, of course, vary wholly with the conditions for which it is done. Thus the nephrostomy done for calculous anuria must be maintained until the calculus causing the obstruction has been removed and until recovery of renal function appears to be satisfactory. Such drainage might continue for from 3 to several weeks. In the same way, the nephrostomy which is done in connection with plastic operations on the renal pelvis will be continued until it is judged that the healing of the operative wound has become satisfactory. Finally, nephrostomy which is done in connection with the removal of renal calculi will vary in its duration according to the condition of the kidney and according to the development of our belief that nephrostomy with its attendant possibilities of altering the physical conditions within the kidney may be used to affect the rapidity or probability of recurrence of stone.

NEPHROSTOMY VERSUS PYELOSTOMY

It will be proper at this time to indicate our opinion of the relative value of nephrostomy and pyelostomy as a method of temporary drainage. In the presence of a distended renal pelvis and particularly when that structure has been opened for the removal of calculi, drainage of the renal pelvis has been regarded as the obvious and simple method. It is, we believe, open to certain objections which have in our experience considerably limited its use. It is much more difficult to retain the drainage tube accurately in the renal pelvis if drainage is to be continued for more than 1 or at most 2 weeks. The accurate replacement of the tube is difficult and not rarely impossible and it commonly occurs that a tube slips out of the pelvis before satisfactory drainage has been accomplished, cannot be accurately replaced, and drainage has to be abandoned. It has also been common in our experience that although the drainage tube may remain in satisfactory position for a matter of 10 days or 2 weeks when it is desired to remove it and replace it by another tube, such replacement has been inaccurate and the result unsatisfactory. The operation has been regarded as desirable because it did not injure renal tissue, did not expose to the same danger of fulminating renal infection as might occur in an infected kidney, and was in all respects a much less serious procedure. We hope to be able to show that nephrostomy may be done by methods which will make it a quite trivial procedure and much less exposed to the above mentioned objections than when carried out by methods more generally in use. On the whole, we incline to the opinion that pyelostomy has a much more limited scope than nephrostomy and one which will tend to become even more limited in the future.

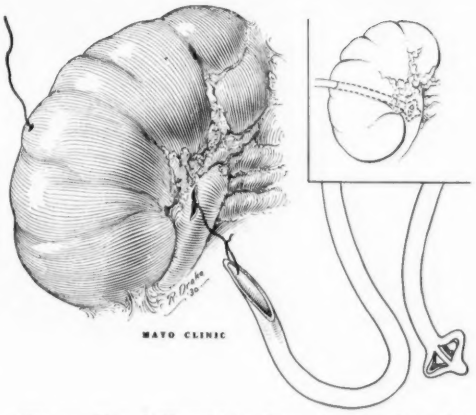

Fig. 10. Use of silk guide to draw winged catheter into proper position in renal pelvis.

SUMMARY OF CASES OF NEPHROSTOMY

During the last year we have performed nephrostomy in 33 cases and these may be used to illustrate our suggestions in regard to its application.

Nephrolithiasis. In this group there have been 14 cases of which 7 were instances of bilateral stone. There were 6 instances of unilateral stone with seriously injured kidneys in which the method was employed in the attempt to preserve the kidney. One was a case of a single remaining kidney, the other having been previously removed elsewhere for calculous disease. The patient had had two recent attacks of calculous anuria.

In all of the cases of bilateral nephrolithiasis the urine was seriously infected. Two patients had been previously operated on with rapid reformation of the stone; the renal function of both, as measured by the return of phenolsulphonephthalein, was markedly below normal. The operation was used in all these cases as a method of attempting to improve renal function and, by local treatment of the renal pelvis, to alter perhaps the rapidity of recurrence (Fig. 1). In all cases the immediate results were satisfactory. We cannot, of course, form any judgment as to the late results. In some cases the condition of the kidney at operation seemed very bad, yet we hesitated to do nephrectomy on account of the condition of the other kidney. It was surprising to note that in 3 cases, kidneys which at operation apparently contained nothing but stones and pus, within 24 hours were putting out a normal quantity of fairly satisfactory urine, both from the point of view of appearance and the point of view of function (Fig. 2). At least as a temporary measure nephrostomy in these cases seemed well worth while.

In 3 of the 6 unilateral cases stones were firmly impacted in the upper part of the ureter with no clear evidence of renal function on that side (Fig. 3). However, at operation the amount of remaining renal substance seemed too great to sacrifice and nephrostomy appeared to show that this judgment had been sound. In the 3 other cases the stones lay in pelvis or kidney, but again the amount of remaining renal tissue seemed too great to sacrifice although the function was very poor before operation (Fig. 4). This small experience suggests to us that this method may permit the retention of a certain number of kidneys which have heretofore commonly been removed on account of the evidence of injured function. In the present state of our knowledge, it is doubtful whether we have any test of the function of a stone-containing kidney on which we can rely as an indication of the permanent function of that kidney.

The remaining case in this group was that of a woman whose left kidney had been removed elsewhere 3 years ago on account of stone. During the last year she had had two attacks of anuria. Before operation the total renal function was below 20 per cent although there was no elevation of nitrogen in the blood. Operation revealed a much dilated and apparently considerably injured kidney, but after nephrostomy this kidney drained freely, its function improved, and 4 months later the output of phenolsulphonephthalein was 40 per cent. In this case the nephrostomy was made permanent.

Hydronephrosis. We include here 5 cases of hydronephrosis apparently due to congenital anomalies in which plastic operations were done on the renal pelvis. In these cases temporary nephrostomy was done in order to allow time for accurate healing of the wound of the pelvis (Fig. 5). In all of these cases the tube was removed in between 2 and 3 weeks, and the condition of the kidney at that time seemed satisfactory. This method has seemed to us preferable to draining through the pelvis in such cases and we believe that some method of drainage other than that which can be obtained through a ureteral catheter is desirable.

Lesions of the nerves. The next group is composed of 4 cases of obscure neurologic lesions resulting in failure of the urinary musculature apparently throughout. In these cases nephrostomy was resorted to in the hope of stopping progressive renal injury. One was the case of a man aged 24 years, whose difficulty apparently followed a gunshot wound of the abdomen. There was extensive pyonephrosis on both sides with dilatation of pelves and ureters. Bilateral simultaneous nephrostomy was done after serious renal insufficiency had developed and the concentration of nitrogen and creatinine in the blood was rising. The operation failed to stop the injury and death occurred 2 weeks after operation. Another case was that of a female child aged 3 years with congenital anomalies of the nerve supply and infectious purpura apparently due to bilateral infected hydronephrosis. Her condition was very bad and nephrostomy was done on the left side. It failed to influence the process. Another was a child aged 5 years with a similar lesion but less infection. Nephrostomy was done on the right side with drainage of a much damaged kidney with an enormous ureter. Very marked improvement in general condition took place and the

patient was dismissed with the nephrostomy tube in place. The remaining patient of this group was a man aged 34 years who had had urinary symptoms suggesting extensive infection of the urinary tract for many years. Careful urologic study showed right hydronephrosis with great dilatation of the ureter, but with no clear evidence as to cause other than a congenital nerve lesion. On the left side there was complete duplication of ureter and pelvis with two stones in the lower segment, considerable dilatation of the ureters, but good function. Study 4 months later showed that the function of the right kidney had diminished to almost nothing and the ureter on this side could not be catheterized. In view of the situation on the left side it seemed as if an attempt should be made to retain the right kidney if possible (Fig. 6). Nephrostomy was done and a month later the phenolsulphonephthalein function from this kidney was 20 per cent while that on the left side was 25 per cent. This patient was advised to return for operation on the left side for the removal of stones.

Obstruction of lower ureter. The next group consists of 3 cases of obstruction of the lower part of the ureter. One was a case of bilateral injury to the ureter at the time of an operation for carcinoma of the uterus. In this case bilateral simultaneous nephrostomy was done which gave satisfactory and adequate drainage. This patient was reported to have died 6 months later, probably from malignant disease. Another patient was also the subject of malignant disease of the uterus under treatment with radium. The disease had obstructed the right ureter and destroyed the right kidney more than a year previously. While under treatment with radium here sudden anuria developed and examination showed impassable obstruction of the remaining ureter. Nephrostomy was done within 24 hours with a most satisfactory result. The third patient was a man aged 52 years whose right kidney had been removed for pyonephrosis in 1927. In 1928, he had a perineal operation for prostatic calculi, and in March, 1931, a cautery operation on the neck of the bladder through the urethra. The latter part of April oliguria began to develop and finally anuria, and catheterization of the left ureter was impossible on account of deforming scar. Nephrostomy was done with an excellent result. At the present time, a varying amount of urine is passed from the bladder. The ureter is not entirely obstructed but seems unable to take up its full function. Nephrostomy in this case was done in order to give an opportunity to make any necessary attack on the ureter possible.

Renal infection. The next group includes 3 cases of infection of the urinary tract with extensive renal injury. The first concerned a man aged 45 years with a long history of a painful infection of the bladder with final contraction of the bladder and infection of the upper part of the urinary tract. All methods of treating the bladder were unsuccessful and he suffered from recurrent attacks of renal infection first on one side and then on the other. Cystostomy had been tried and had failed. His condition seemed so bad that the chance of benefit by nephrostomy seemed worth taking. This was done on the right in February, revealing a battle scarred kidney without dilatation but with much thickening of the pelvis and ureter. Following nephrostomy his condition improved very much. Two months later he had relapse of the infection in the left kidney. This, interestingly enough, entirely interrupted the function on that side and for nearly 2 weeks the right nephrostomy carried on total function. Then the infection on the left quieted and the function of that kidney returned with rapid subsidence of the urinary output on the nephrostomized kidney. It is our intention to operate on the left kidney in view of the apparently marked improvement of the condition of the right. This case throws interesting light on the behavior of a kidney during acute infection. Another case was of a somewhat similar type with prolonged infection of the urinary tract, extensive injury to the bladder and ureters with recurrent attacks of renal infection on both sides which had resulted in very grave injury so that there was marked elevation of blood urea and a phenolsulphonephthalein excretion of 20 per cent in 2 hours. Pyelogram of the kidneys showed moderate bilateral infected hydronephrosis. Bilateral nephrostomy was done in two stages and the patient left the hospital a month after the second operation with marked improvement of renal function and in good condition. The remaining case in this group was an obscure one with probable renal tuberculosis on one side and obstruction of the ureter on the opposite side. Nephrostomy was done as an emergency measure for threatened anuria with blood urea of 152 and creatinine of 4 milligrams in each 100 cubic centimeters. Marked improvement occurred after operation and the patient went home with a satisfactorily draining nephrostomy. He died 4 months later, probably of tuberculosis. These cases are introduced simply to indicate a possible field for the use of nephrostomy in the treatment of certain cases of advanced renal infection.

Carcinoma of the bladder. The 4 remaining cases were of patients with extensive carcinoma of the bladder producing ureteral obstruction. Nephrostomy was done as a temporary measure to prolong comfortable existence but without any expectation of prolonged benefit on account of the extensive involvement of the bladder. The results seemed to have justified the operation.

Mortality. In this group the mortality should be credited to the operation in 3 cases. Two patients had extensive bilateral infected hydronephrosis apparently due to abnormality of the nerve supply. The condition of these was desperate and the patients died really of the disease and not of the operation. One of the patients had extensive carcinoma of the bladder in which nephrostomy was done as a late measure. Our experience in regard to mortality is similar to that of all other observers, namely, that the operation itself is relatively safe but as it is frequently done for serious or desperate conditions it will be associated with the mortality properly to be expected in these situations.

Bleeding. Bleeding did not occur following operation.

Infection. We have had no instance of fulminating renal infection although this will doubtless occur in an occasional case in which any operation is done involving the renal parenchyma in the presence of existing infection. The effect of the operation on pre-existing infection has, during this brief period, been satisfactory. There has regularly been prompt improvement of infection although it is of course as yet too early to express any opinion as to the ultimate effect.

Calculus. We feel particularly interested in the patients with bilateral extensive calculous disease, since it seems possible that prolonged drainage of the kidney by this method may preserve waning renal function and may influence the rapidity and extent of stone formation. On this point it is highly desirable that prolonged observation should be made.

TECHNIQUE

In the earlier days the operation consisted of a considerable nephrotomy along the convex border with the division of much tissue to enable the drainage tube to be accurately placed in the pelvis. This method has been practically wholly abandoned and has been replaced first by the method of Marion which introduces a dilator through the cortex of the kidney through which the tube is passed (Fig. 7). Later was developed the method of opening the renal pelvis and passing a curved instrument out through the cortex at the desired point by means of which the drainage tube is drawn down into the pelvis and placed accurately in position. Papin, in 1927, advised the method of Marion for temporary nephrostomy and the method of introducing an instrument into the renal pelvis for permanent nephrostomy. He at that time advised the use of a winged catheter which was important in overcoming the very considerable danger that the tube would become displaced, work gradually out into the substance of the kidney, and finally fail to drain the kidney at all (Fig. 8). One of the common and annoying complications of nephrostomy is this displacement of the tube. There is no structure of the kidney to which a tube can be safely and satisfactorily attached, but the use of a winged catheter seems to overcome this objection and maintain the tube in accurate position until such time as the drainage tract has become satisfactorily established.

The technique which we are suggesting is put forward as an improvement on this latter method. We have encountered a large number, and perhaps a fair proportion of the cases, in which the mobilization of the kidney sufficient to allow a curved instrument to be readily introduced into the pelvis and passed out through the desired point on the cortex is either impossible on account of the fixity of the kidney or involves an amount of preparatory dissection which unnecessarily prolongs and complicates the operation. In not a few of these cases particularly those in which a bilateral simultaneous nephrostomy is indicated the element of time is of importance and it has seemed to us that a method which could be employed without extensive mobilization of the kidney was desirable. There is also a certain number of these cases in which there is no dilatation of the renal pelvis in which it may in fact be entirely intrarenal and in which the introduction of an instrument as illustrated by Papin has in our hands been difficult.

The method which we suggest is as follows: The kidney having been exposed and mobilized to an extent to give access to the upper part of the ureter and the renal pelvis, a small opening is made in the pelvis, although in the case of the intrarenal pelvis it may actually be made in the ureter. A uterine sound with a slightly bulbous tip bent in "U" shape is introduced into this opening and passed out though the cortex at the point selected (Fig. 9). This point should, we think, be placed so as to drain the lower calyx as the most efficient method of draining the kidney, but it should also be placed in relation to the convex border of the kidney in such a way that

the drainage tube will lead straight from the wound and not be exposed to angulation as the kidney falls back into its normal position. This point can be readily ascertained by seeing where the kidney will most comfortably lie, and the sound, which has been introduced into the pelvis, is pushed out through the cortex at that point. A piece of stout silk is then attached to the bulbous tip, withdrawn through the kidney and out of the opening in the pelvis and to this is attached the winged catheter (Fig. 10). As a rule we use a winged catheter of no. 22 to 24 French. The end of this catheter should be trimmed off to a point. Traction on the suture then draws this catheter accurately along the line created by the sound, and it fits so tightly in the renal parenchyma that bleeding will be entirely controlled. As a rule we have not thought it necessary and perhaps not wise to close the small opening made in the renal pelvis but have allowed this to remain until it closes spontaneously, which will as a rule take place within a week. This winged catheter is not fastened to the kidney or to any portion of the overlying tissues and the kidney is thus allowed to decide for itself, so to speak, the position in which it prefers to lie. The drainage from these catheters has been eminently satisfactory. Experience has led us to the opinion that they should be left in place for about 2 weeks at which time a straight tube can be substituted. For this purpose we use a no. 22 rectal tube which has an opening in the end and in the side. The removal of the catheter is facilitated by passing through it a stilette when traction on the catheter will smooth out the wings of the catheter so that it does not lacerate the renal tissues. If the straight tube is immediately replaced and if care is taken to see that it penetrates for exactly the same distance, most satisfactory drainage can thus be obtained. After the first change there has been no subsequent difficulty and after a few weeks the patient can as a rule have the tube changed by some member of the family.

This technique seems to us to involve less injury to renal tissue than previous methods. By drawing the tube outward through an opening much smaller than its own dilator the oozing from the renal parenchyma is entirely controlled. We have seen little if any bleeding following the procedure and have as yet seen no immediate or fulminating infection although it may be admitted that any laceration of the renal parenchyma will under suitable conditions of previous infection give rise to this dread complication.

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NUPERCAINE SPINAL ANÆSTHESIA

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THE following is a report of the experience with the use of the drug "nupercaine" (Ciba) in spinal anæsthesia at the Mount Sinai Hospital in New York City. This drug, known as "percaine" in Europe, has been used extensively as a local anæsthetic, but this report will be confined to its use in spinal anæsthesia.

Chemical and physical properties of nupercaine. Nupercaine is a quinoline derivative—alpha-butyl-oxy-cinchoninic acid diethyl-ethylene-diamide hydrochloride. It occurs in the form of colorless crystals which are readily soluble in water. Distilled water and chemically pure sodium chloride should be used for preparing the solutions. These solutions may be boiled repeatedly without decomposition. Very slight alkalinity decomposes the salt with precipitation of the base. Thus it is essential that no alkali come in contact with the solution. Any alkalinity derived from glass containers may be counteracted by adding 5 minims of dilute hydrochloric acid to each liter of solution. The drug is manufactured in convenient ampules of 2 cubic centimeters of 1:200 in a buffered sodium chloride solution for use in spinal anæsthesia.

Toxicity of nupercaine. From investigations on laboratory animals reported by Uhlmann, Lipschitz and Laubender, Gessner and Nauheimer, and more recently by Bond and Bloom, it is evident that nupercaine in certain concentrations is a toxic drug. The toxicity varies from two to five times that of cocaine. On the other hand, when solutions of nupercaine and cocaine are injected subcutaneously into dogs it would seem that the toxicity of the two substances is practically the same (Bond and Bloom). This may be explained by the fact that the subcutaneous fatal dose of nupercaine is approximately eight times the intravenous dose, whereas with cocaine the ratio of subcutaneous and intravenous toxicity is two to one. An absolute comparison of the relative safety of nupercaine and other local anæsthetics in man requires further clinical experience. It should be noted that, being a very powerful anæsthetic agent, ten times as anæsthetic as cocaine, nupercaine is effective in such high dilutions that toxicity in practical use is reduced to a minimum. Nupercaine is rapidly eliminated or detoxicated by the body (Bond and Bloom). The mechanism of elimination of the drug has not been sufficiently investigated. It is believed that the liver plays an important part in its destruction.

The following deaths after injection of nupercaine into the spinal canal are taken from the literature:

1. Heckenbach has reported in a patient, 38 years old, respiratory paralysis shortly after the supposed administration of a paravertebral anæsthesia prior to a ureterotomy for calculus. He interrupts the eleventh and twelfth dorsal and first lumbar with 10 cubic centimeters of a 0.1 per cent solution each. The patient died 15 minutes later. The supposition that inadvertently an intralumbar injection had been made was confirmed by the autopsy, at which time the insertion into the spinal canal could be incontestably demonstrated.

2. W. H. Jones (13) reported the death of a woman, 50 years old, with a multilocular ovarian cyst extending to the costal margin. She was given 14 cubic centimeters of 1:1500 solution of nupercaine between the first and second lumbar vertebræ, and then placed in the ventral position to allow the light nupercaine solution to come into contact with the dorsal roots. In about 3 minutes collapse occurred. The patient was then turned on the back and the cyst punctured after the abdomen was opened with the object of removing pressure on the diaphragm. This was of no avail. Autopsy was negative except for the condition previously mentioned.

Jones is of the opinion that the ventral position in patients with large abdominal tumors is a mistake, pressure on the diaphragm being transmitted to the heart. He feels that the small amount of nupercaine, about 9 milligrams, could not exert a systemic action sufficiently great to cause death.

3. Steinbruck reported the death of a 60 year old man with a diffuse peritonitis after a spinal injection of 1.5 cubic centimeters of a 1 per cent solution of nupercaine.

4. Keyes and McLellan (15) reported two deaths. The first case was that of a patient with anuria-blood nonprotein nitrogen, 99 milligrams per 100 cubic centimeters, creatinin, 6.4 A left nephrectomy had been performed at the age of 12. Operation revealed the remaining kidney to be sclerotic and contracted. The pre-operative systolic blood pressure was 110. The patient died one hour after the injection of 2 cubic centimeters of 1:200 solution of nupercaine. There was no postmortem examination.

5. The second case was a cardiac failure on the operating table during a prostatectomy after the injection of 2 cubic centimeters of 1:200 solution of nupercaine. The pre-operative blood pressure was 120-80. There was no postmortem examination.

6. At a meeting of The American Society for Regional Anesthesia in February, 1931, M. Weinstein reported a death in a case of cæsarean section in a very obese woman of 28 years of age. Two cubic centimeters of 1:200 solution of nupercaine was injected at the level of the second lumbar vertebra with the patient in the sitting posture. About 8

minutes after the injection the patient ceased breathing before the operation had started.

REVIEW OF LITERATURE

The first clinical report on the use of nupercaine was that of Christ. He stated that good spinal anæsthesia was obtained with 4 cubic centimeters of 1:1000 solution. General toxic reactions were not observed.

De Weerdt has employed nupercaine for spinal anæsthesias in 151 cases for all sorts of operations. He noted that anæsthesia and paralysis of the legs occurred some minutes later than with other anæsthetics. There were often some sensitive zones, the cause of which was probably due to improperly prepared solutions. The patients looked better than when other anæsthetics were used. Vomiting occurred less frequently. A sudden cardiac weakness occurred in some cases a few minutes after the injection, but this was successfully combated by means of intravenous injections of caffeine. He commented on the long duration of the anæsthesia, and was well satisfied with his results.

Eichhoff's experience with nupercaine in various strength solutions for spinal anæsthesia in 9 cases, was rather unsatisfactory. The experience of Floercken and Mues with nupercaine spinal anæsthesia was unsatisfactory. In 3 cases, 4 cubic centimeters of 1:1000 solution produced a good low anæsthesia; in 7 additional cases it was entirely inadequate; in 2 cases 1 cubic centimeter of 1 per cent solution was followed by severe collapse in 1 case and insufficient anæsthesia in the other.

Iwata employed nupercaine in 20 abdominal operations, 4 to 5 cubic centimeters of 1:1000 solution being used. There was complete anæsthesia in 16 cases, in one instance sufficient for an operation lasting 1 hour, 46 minutes. In the 4 remaining cases, there was a suspicion that the syringe was not alkali free. In one of these cases inhalation anæsthesia had to be used. Twelve patients had no postoperative pain. Headache was never observed, but some gastric discomfort and vomiting occurred generally the day after operation.

Jastram reported his experiences with nupercaine for spinal anæsthesia in 12 cases. The anæsthesia lasted at least 5 hours. He used 0.75 to 1 cubic centimeter of 1 per cent solution.

W. H. Jones has employed nupercaine for spinal anæsthesia in over 200 cases. He used the higher dilutions of the drug, the duration of the analgesia being proportional to the concentration of nupercaine. For operations of about three-fourths of an hour, 1:2000 was effective; for 1 hour or more, 1:5000; for 2 hours and beyond, 1:1000. The maximum dosage was 18 milligrams, although 7½ milligrams was satisfactory for most laparotomies. For anæsthesia of the dorsal roots, the injection was made between the first and second lumbar vertebræ; for anæsthesia of the sacral and coccygeal plexuses, between the first and third lumbar vertebræ; and for blocking of the cauda, between the fourth and fifth lumbar vertebræ. Only a few drops of cerebrospinal fluid were allowed to escape, and the solution was injected directly. The patient was then turned directly on his face for about 5 to 10 minutes or even longer if the operation was likely to be prolonged. Jones did this because he found that many of the nupercaine solutions used had a specific gravity less than that of the cerebrospinal fluid, and in the dorsal decubitus there is therefore a predominating anterior root block with little or no effect on the posterior roots. Thus the entire abdominal musculature may be paralyzed, and yet the anæsthesia be a poor one. The patients were therefore placed in the ventral decubitus in order to soak the posterior roots and develop analgesia, and when patients were finally put in the dorsal position, paralysis of the anterior roots would naturally follow and would outlast the analgesia if the time allowance on the posterior roots had been too short. Jones noted a fall in blood pressure due to vasomotor paralysis, but the fall was not nearly so great as with large doses of novocain or stovaine. The patient's color and appearance were usually excellent. He claims that this relative non-toxicity is not a property of the pharmacological action of nupercaine, but is due to its high dilution which makes sudden absorption into the blood stream impossible. Spontaneous vomiting was rarely seen on the operating table for this reason. There may develop some degree of respiratory embarrassment, due to a paralysis of the intercostal nerves owing to the predominating anterior root effect of the nupercaine solution. Jones states that failures with nupercaine mean faulty administration. In discussing the after-effects of the anæsthesia, Jones states that the usual spinal headache had followed in several cases, sometimes severe and lasting several days, but no more so than with solutions of novocain. Several cases of severe vomiting occurred early in the series, but this number has decreased. The incidence of headache and vomiting had no direct relationship to the amount of nupercaine injected. In this report there had been no fatalities. The report of a death in a later series has been discussed previously.

The first report in the American literature was that of Keyes and McLellan (14). They used nupercaine for spinal anæsthesia in 46 cases. High dilutions of the drug were first used, but the dosage used in 28 cases was 2 cubic centimeters of 1:200 solution (10 milligrams). No intoxications or paralyses were observed. There was one spinal headache. The anæsthesia was used in 24 suprapubic bladder operations, 9 kidney operations, 11 urethral and intravesical operations, and in 2 patients in whom spinal anæsthesia was used to control renal colic. The anæsthesia was perfect in 36 cases, and had to be supplemented in 10 cases. No alarming symptoms were observed during operation. Vomiting during the operation did not occur, and only 3 patients vomited thereafter. The systolic blood pressure of 29 patients fell an average of 18 points; that of 11 others did not fall. The maximum fall was 70 points. Ephedrine was used in all cases. The duration of anæsthesia varied from 1½ to 12 hours, the average being 7 to 8 hours. Nine patients did not complain of any postoperative pain, but all open operations required sedatives the following night. Accurate studies of blood pressure changes were made in 41 cases, and compared to procaine (120 milligrams) and spinocaine (200 milligrams). The average maximum fall in blood pressure after procaine was 31 millimeters, after spinocaine 39 millimeters, and after nupercaine 18 millimeters. There was a rise in blood pressure above the ante-operative pressure in 11 nupercaine cases, 4 procaine cases, and 3 spinocaine cases. The blood pressure began to return to normal as soon after nupercaine as it did after procaine, and an initial sharp drop in pressure after nupercaine did not usually imply a further drop of 30 to 50 millimeters as would be the case after procaine. No deaths were reported.

At a recent meeting of the American Society for Regional Anæsthesia in February, 1931, McLellan (15) reported on further experiences with nupercaine. He reported 215 anæsthesias in 159 patients. The highest anæsthesias were for kidney operations—41 cases. The remainder were for operations below the umbilicus. Two-thirds of the patients were below 50 years of age—the youngest 16 and the oldest 80. The dosage used was 10 milligrams, 2 cubic centi-

meters of 1:200 solution. All patients received 50 milligrams of ephedrine before operation. In all the cases the injection was made between the third and fourth lumbar vertebræ with the patient in the sitting position. The height of the anæsthesia varied with the amount of cerebrospinal fluid withdrawn. For kidney operations, 8 cubic centimeters of fluid was added to the nupercaine. In 3 instances the anæsthesia extended to the clavicle. The number of falls in blood pressure was less than with procaine. In younger people, the pressure often remained at or above normal. In older people, the fall in pressure was greater, but this fall was no more prolonged than with procaine. On the operating table, vomiting occurred four times. Respiratory paralysis occurred twice—1 patient recovered and 1 died. There was one postoperative headache. In 16 instances the anæsthesia had to be supplemented with a general anæsthesia. Two deaths were reported. These are discussed above.

At the same meeting M. Weinstein reported nupercaine spinal anæsthesia in 43 instances. Four of these cases were over 50 years of age. No ephedrine was used before operation. The dosage of the drug was 10 milligrams, 2 cubic centimeters of 1:200 solution. The anæsthesia sets in from 3 to 10 minutes after the injection. In some cases the patients complained of pain at the beginning of the operation which wore off later. In all cases relaxation was good. The anæsthesia lasted from 2 to 4 hours. No essential differences could be determined between the number and extent of falls in blood pressure compared to neocaine. Nausea in 12 to 24 hours occurred in 73 per cent of the cases, and vomiting in 6 to 12 hours in 63 per cent of the cases. In 2 cases there were evidences of cerebral irritation as manifested by delirium, tremor, or convulsions. Thermal reactions were noted, usually 6 to 8 hours after operation, a chill usually preceding the rise in temperature. Headache within 2 to 4 days was noted in 72 per cent of the cases. There were many instances of posterior cervical rigidity. There were no disturbances in urination or defæcation, and no peripheral nerve palsies. The death reported has already been discussed.

Von Konrad reported his observations on the use of nupercaine spinal anæsthesias in 73 cases. The dosage used was 8 milligrams. A lowering of the blood pressure did not occur even when ephedrine was not given before operation. Complete anæsthesia of long duration was observed. The duration of the anæsthesia amounted to an average of 4 hours and 36 minutes. The shortest was 2½ hours, and the longest 6¾ hours. Anæsthesia set in about 5 minutes after the injection. The disappearance of the anæsthesia proper was followed by a condition of greatly decreased sensitiveness to pain. This period lasted from 5 to 8 hours, and occasionally even longer. The observation was also made that 1½ to 2 hours after operation, a fairly marked intestinal peristalsis set in, especially marked in the so called "subanæsthetic stage." This postoperative "reactive" condition of the intestines lasted 24 to 48 hours. The so called "lumbar reaction" was slight. Temperatures of 100.4 to 100.6 degrees were reached only rarely. The pulse frequently varied in its maximum between 90 and 98. The entire "lumbar reaction" itself had run its course after 24 hours, and the patients during this time created a considerably fresher impression than those after a lumbar anæsthesia with the cocaine derivatives. Collapse was never observed, either after the completed lumbar injection or during or after the anæsthesia. Vomiting and headache were never observed. Nupercaine did not influence the respirations either during or after the operation. Nupercaine may be employed in severely anæmic patients, in pregnant women, and in women during labor, since the drug in the dose suggested had no harmful effect on the blood pressure. "At the present time nupercaine may be regarded as the best lumbar anæsthetic."

During the period of a year, Quarella had employed nupercaine for spinal anæsthesia in 400 cases. He constantly obtained, in abdominal operations, a complete analgesia of long duration and a complete relaxation of the muscles. Only two cases of the series showed phenomena of collapse of any seriousness. In both cases, the preoperative injection of ephedrine had been neglected. The dose recommended is 10 milligrams, although 15 milligrams had been given without unpleasant reactions. In accord with other authors, he noticed that the individuals operated upon under spinal anæsthesia with nupercaine were in a much better general condition during the operation as well as after than those in whom novocain or tropococaine had been used. The headaches after spinal anæsthesia, especially those severe forms of long duration, had been much more rare with nupercaine than with the other anæsthetics. No paralysis or paresis of cranial nerves, especially of the abducens, had been observed.

Steinbruck reported on the use of 1 per cent solution of nupercaine in 12 cases for spinal anæsthesia. He generally used 0.75 to 1 cubic centimeter because he noted collapse in 1 case following the injection of 1.4 cubic centimeter, and the death of another patient, a 60 year old man with diffuse peritonitis, following the injection of 1½ cubic centimeters.

Take and Shimizu have employed nupercaine for spinal anæsthesia in the dose of 1 to 2 cubic centimeters of a 1:200 solution. No toxic manifestations of any sort were observed, and the anæsthesia was most satisfactory.

Thomas used nupercaine as a spinal anæsthetic in 80 cases. Of the operations, 41 involved abdominal section. In no case was there any fault to find as regards complete musculature relaxation, but in 5 a little supplementary anæsthetic had to be given. Vomiting occurred only during traction on the stomach in some of the upper abdominal operations. With the usual dose, the anæsthesia usually persisted for about 5 hours. The longest operation took 3 hours. The solution used was 1:1500 in 0.5 per cent saline. The amount injected was 10 to 20 cubic centimeters. A fall in blood pressure of 10 to 20 millimeters occurred in 54 per cent of the cases, but returned to normal before the operation was over. In the other 46 per cent, there was no alteration of blood pressure. Spinal headache occurred with varying degrees of severity in a few cases. No deaths were reported.

Ziegner has employed 1 per cent solution of nupercaine for spinal anæsthesia in a total of 54 patients. He advised that a dose of 10 milligrams should not be exceeded, and he preferred to use 8 milligrams. He had observed no untoward results with nupercaine and preferred it to other anæsthetic agents because of the long duration of the anæsthesia.

The following is a report of the experience with the use of nupercaine in spinal anæsthesia at the Mount Sinai Hospital in New York City.

Age distribution in years	Cases
10 to 20	2
20 to 30	10
30 to 40	26
40 to 50	30
50 to 60	29
60 to 70	21
70 to 80	2
Total cases	120

Sex distribution: male, 84; female, 36.

TECHNIQUE

In most cases, the individual surgeon acted as his own spinal anæsthetist, the patient being carefully observed throughout the course of the operation by a regular nurse staff anæsthetist.

Dosage of drug. In nearly all cases, the dose of nupercaine was 10 milligrams—2 cubic centimeters of 1:200 solution. In 3 cases, the dose was 7½ milligrams, and in 1 case, 5 milligrams.

Position of the patient. The lumbar puncture was done with the patient either in the sitting or in the lateral position. Immediately after the injection, the patient was placed in slight Trendelenburg position.

Preliminary medication. Morphine and atropine were administered prior to the procedure in nearly all cases, and codeine and atropine in a few. Ephedrine was given in 101 cases. The usual dose of ephedrine was 50 milligrams.

Level of injection. The level of injection was specifically noted in 60 cases. In 14 of these, the injection was administered above the second lumbar vertebra and in 46 below that site.

Blood pressure changes. Accurate blood pressure determinations were recorded in 84 cases. In 66 cases there was a fall in blood pressure of from 10 to 150 millimeters of mercury. This fall occurred in most cases within 15 minutes following the injection of the anæsthetic. Marked drops in blood pressure (50 millimeters or more) were noted in 26 cases. In nearly all cases in which a fall in blood pressure was observed, ephedrine had been used prior to induction. In 16 cases there was a rise in blood pressure which was maintained above the ante-operative blood pressure throughout the course of the operation. The rise in most cases was within the first 10 minutes. Ephedrine was used in all these cases. In 2 cases there was no change in the blood pressure.

We were particularly interested in the blood pressure changes in patients with hypertension (systolic blood pressure above 150 millimeters) and hypotension (systolic blood pressure below 100 millimeters). Of the 10 patients with hypertension, 9 had falls in blood pressure of from 50 to 150 millimeters of mercury. All of the 4 patients with hypotension had a rise in blood pressure of from 20 to 40 millimeters of mercury. From this and other studies we are loath to use spinal anæsthesia in patients with marked hypertension. Marked drops in blood pressure in these patients are often accompanied by severe clinical manifestations. On the other hand, we do not feel that hypotension, in itself, is ever a contraindication to spinal anæsthesia.

No relation could be determined between the changes in blood pressure and the level of the injection. Striking falls in blood pressure were observed as frequently in injections below the second lumbar vertebra as in those injected above that level.

Adequacy of anæsthesia. The anæsthesia was considered adequate throughout the operation in 110 cases (91.6 per cent). No supplementary anæsthesia was used in this group. The duration of operation of these 110 cases was as follows: 58 cases were under 1 hour; 37 cases were between 1 and 2 hours; 15 cases were between 2 and 3 hours. The longest operation was of 3 hours' duration. The actual duration of anæsthesia beyond the operative time was only rarely noted. We have records of anæsthesia lasting 4 and 6 hours.

The spinal anæsthesia had to be supplemented in 4 cases (3.3 per cent)—1 in the first hour, and 3 in the second hour.

The anæsthesia was entirely unsatisfactory in 6 cases (5 per cent). In 3 of these, we know that the technique of injection was faulty.

These figures compare very favorably with statistics we have recently compiled in an analysis of 497 instances of spinal anæsthesia in which neocaine was used as the spinal anæsthetic agent. In that series, in 65.6 per cent the anæsthesia was adequate, in 32.8 per cent it had to be supplemented, and in 1.6 per cent it was unsatisfactory.

There were 17 patients who complained of varying degrees of discomfort, not severe enough to require a supplementary anæsthesia, but in whom the muscular relaxation was good. In these cases there was a predominating anterior root block with little effect on the posterior roots. Jones tries to avoid this by turning his patients directly on the face for about 5 or 10 minutes before they are placed in the dorsal position. This is particularly necessary, he claims, where nupercaine solutions of a specific gravity less than that of the cerebrospinal fluid are used.

Untoward reactions. Untoward reactions on the operating table were noted as follows: vomiting in 4 cases; respiratory failure (with recovery) in 1 case; signs and symptoms of shock, in 10 cases. As noted elsewhere (1), the latter occurred for the most part, in patients in advanced years who showed evidences of arteriosclerosis and myocardial disease, or in those cases of cachexia or intoxication from some debilitating disease.

General condition of the patient before operation. A large variety of medical complications was found in the group of patients under consideration. The most outstanding are shown in Table I.

TABLE I

	No. of patients
Anæmia (hæmoglobin below 60 per cent)	12
Obesity	12
Arteriosclerosis (generalized)	12
Chronic bronchitis and emphysema	11
Hypertension	10
Hypotension	4
Cachexia	4
Jaundice	3
Uræmia	3
Chronic cardiac valvular disease	3
Coronary artery disease	2
Pulmonary tuberculosis	3
Diabetes	2
Chronic nephritis	1
Syphilis	1

Nature of operation. Types of operation:

	Cases
Stomach (25 gastrectomies)	30
Kidney and bladder	23
Intestinal (including appendicectomies)	19
Liver and biliary passages	19
Hernioplasties	10
Exploratory laparotomies	9
Rectal and rectosigmoidal resections	6
Anal	1
Splenectomy	1
Gynecological	1
Extremities (lower)	1

Complications. The following are complications which we feel are in some degree attributable to the spinal anæsthesia.

1. Headache, lasting from 1 to 5 days, was noted in 19 cases (15 per cent).

2. Signs of meningeal irritation in the form of rigidity of the neck and a positive Kernig sign were found occasionally—the former in 12 cases, and the latter in 6 cases.

We have no accurate record of the number of cases in our former series of neocaine spinal anæsthesias showing these subjective and objective signs of meningeal irritation, headache, rigidity of the neck, and Kernig sign, but it is our impression that such manifestations were not as frequent with neocaine. At a recent meeting of the American Society for Regional Anæsthesia in February, 1931, McLellan reported one headache in 215 cases (0.4 per cent), while M. Weinstein reported 31 headaches in 43 cases of spinal anæsthesia (72 per cent). Equally contradictory reports are found throughout the literature.

3. Peripheral nerve palsies were noted in 2 cases—in both cases being an involvement of the sixth, abducent, nerve.

4. In 5 cases, there were signs of cerebral irritation. Some of these patients had varying degrees of disorientation and mental excitability. In 1 case, which will be described in detail below, the patient had delirium and convulsions.

5. Thermal reactions were noted in 6 cases. The exact mechanism of these reactions is difficult to explain. In 1 case, to be described, the hyperpyrexia was extreme, reaching 109.4 degrees.

Vascular complications. In a previous paper (1) we noted that after a spinal anæsthesia, patients with hypertension may develop suppression of urine as a result of marked drops in blood pressure when not overcome. The following is a brief report of a case presenting another complication, secondary hæmorrhage, attributable to a marked fall in blood pressure.

A man, 63 years of age, with arteriosclerosis, obesity, and emphysema, was admitted to the hospital with a large, irreducible, recurrent, scrotal hernia. Operation was performed under nupercaine spinal anæsthesia. The preoperative blood pressure was 146-80. The immediate drop in pressure was so great that it could not be recorded. After that it rose to the highest level of 80-60. The operative field was bloodless, not a single vessel being ligated. Six hours after operation, the blood pressure was 140-90, at which time the dressings were blood stained. He developed pulmonary œdema and died on the second day after operation. At postmortem, a hæmatoma at the operative site, the scrotum, and the right flank, was found due to unligated branches of the inferior epigastric artery. In addition, there was an acute purulent bronchitis, pulmonary œdema, and atelectasis.

Pulmonary complications. In the paper referred to, we noted a relatively high incidence of postoperative pneumonias (4.2 per cent). In this series there was a still higher incidence, 10 cases (8 per cent). Spinal anæsthesia does not prevent postoperative pulmonary complications. After operations on the upper abdomen, particularly, patients are liable to these complications, whatever the form of anæsthesia.

Deaths. The following is the report of a case in which the spinal anæsthesia was probably a contributory cause of death.

The patient was a young man of 19 years, admitted to the hospital with a history of abdominal pain, nausea, vomiting, fever, and chilly sensations for 7 hours. He had had a similar attack 3 months before. Four months before admission, he had had fever and joint pains, said by a doctor to be rheumatic fever. Physical examination showed a well developed boy, acutely ill, with temperature of 101 degrees. Signs of an acute appendicitis were present, in addition to a severe acute nasopharyngitis. There was a loud systolic murmur at the cardiac apex. In view of the acute nasopharyngitis and the rheumatic manifestations, a spinal anæsthesia was given, 10 milligrams of nupercaine being used. An acute, phlegmonous appendicitis was found, and the appendix was removed. The anæsthesia was satisfactory, and there were no untoward signs during the operation. The pre-operative blood pressure was 116-80, dropping to 100-65 in 15 minutes, and rising to 120-80 by the end of the operation. The patient's condition was entirely satisfactory until 5½ hours after operation, when he suddenly went into a furious maniacal delirium, requiring several persons to hold him in bed. He cried out continuously, but was unconscious and un-

responsive. Sedatives were of no avail. After 2 hours of struggling, he quieted down. His temperature at this time was 109.4 degrees. He was now stuporous with very rapid respirations. The pulse was rapid but of good quality. Continuous spongings brought his temperature down to 106 degrees. About 7 hours after the onset of his seizure, the quality of the pulse became poor. The temperature at this time was 107.2 degrees. He received stimulation but died 2 hours later, about 14 hours after operation.

Postmortem examination showed hæmorrhagic bronchopneumonia of all lobes of the lungs, acute congestion of all the viscera, a persistent thymus, subendocardial hæmorrhages, chronic valvular disease of the mitral valve, rheumatic endocardial lesion of the left auricle. Gross examination of the brain showed no abnormalities. Microscopic sections of the cortex showed thickening with infiltration of the meninges with leucocytic elements, chiefly polymorphonuclears. Sections of the hypothalamus showed a similar exudate with some evidence of early organization. The adjacent parenchyma showed perivascular infiltration with mononuclear and polynuclear elements and also some extravasated blood. Diagnosis: meningo-encephalitis.

The interpretation of these lesions of the brain is not clear. Dr. J. H. Globus, neuro-pathologist at the Mount Sinai Hospital, thinks it unlikely that lesions of this nature could have arisen in the short postoperative course and possibly a cerebral lesion existed before operation.

SUMMARY

1. Nupercaine is a quinoline derivative which may be boiled, is decomposed by alkali, is ten times as anæsthetic as cocaine and about twenty times as anæsthetic as procaine, and is rapidly detoxicated by the body.

2. Five deaths taken from the literature and one unpublished fatality are reported following the use of nupercaine spinal anæsthesia.

3. A review of the literature shows, in general, a satisfactory anæsthesia of long duration, from two to six times that of procaine.

4. This is a report of the use of nupercaine in spinal anæsthesia in 120 cases.

5. The dose recommended is 10 milligrams—2 cubic centimeters of 1:200 solution.

6. Blood pressure fell in about the same number of cases as with procaine (78 per cent of this series). These falls in blood pressure are most marked in patients with a previous hypertension and minimal in those with a previous hypotension.

7. The anæsthesia was adequate in 110 cases (91.6 per cent), unsatisfactory in 6 cases (5 per cent), and had to be supplemented in 4 cases (3.4 per cent).

8. The anæsthesia was of long duration, occasionally lasting 4 to 6 hours.

9. Pronounced reactions on the operating table occurred, for the most part, in patients in advanced years who showed evidences of arteriosclerosis and myocardial disease, or in those cases of cachexia or intoxication from some debilitating disease.

10. Signs of meningeal irritation are more frequent with nupercaine than with procaine.

11. Signs of cerebral irritation and thermal reactions are occasionally noted after operation.

12. There was a high incidence of postoperative pneumonia, 8 per cent.

13. One fatality is reported in which the spinal anæsthesia was a contributory cause of death.

CONCLUSION

Nupercaine is a good anæsthetic agent for spinal anæsthesia, and is especially indicated in operations of long duration.

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JAUNDICE CAUSED BY PANCREATIC LESIONS

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WE have distinguished three types of jaundice: hæmolytic, intrahepatic, and that due to obstruction of the extrahepatic bile ducts. In the last group, jaundice may be due to obstructing stones, to strictures, or to tumors of the head of the pancreas which may be either malignant or inflammatory. In obstruction of the pancreatic portion of the common bile duct, anastomosis between the gall bladder or common bile duct on the one hand and the stomach or duodenum on the other, suffices to relieve the obstruction and to re-establish the continuity of the biliary and intestinal tracts. This operative procedure is encouraged by the marked distention of the gall bladder and the bile passages in such cases.

We are presenting a study of 113 cases in which lesions of the pancreas have produced obstruction of the bile ducts sufficient to produce jaundice. The patients were all operated on at The Mayo Clinic; cholecystenterostomy was performed. Fifteen per cent of the patients who recovered from the operation lived longer than 5 years after operation. Of these, 2 patients are living 13 years; 1, 9 years; and 2, 8 years. The supposition is that in the cases in this group in which the patients lived longer than 5 years, the obstructing pancreatic lesion was inflammatory. Supporting this are the microscopic observations in a group of 25 cases in which tumors in the head of the pancreas produced obstructive jaundice; in 4 of these, the pancreatic lesion was found to be inflammatory, and in the remaining 21 malignant.

The inflammatory type of obstruction has been called a part of a panbiliary infection by Hartman. The obstruction may be localized in the head of the pancreas or in the walls of the biliary passages. In a study of 1,027 cases in which operation for disease of the biliary tract was performed at The Mayo Clinic in 1922, Hartman found that in 60, jaundice was due to inflammatory lesions, without biliary calculi. The routes of infection leading to pancreatitis in most instances may be through the lymphatic channels from the gall bladder or duodenum, or infection may be hæmatogenous. If the pancreatitis is mild and does not cause marked obstruction of the common bile duct, cholecystectomy and temporary drainage of the common bile duct usually suffice to relieve the pancreatitis. Schmieden instituted drainage of the common bile duct in 139 of 308 cases. He effected anastomosis of the biliary and intestinal tracts in 50 cases, made incisions of the pancreatic capsule in 106, and incisions of the glandular tissue in 27. He reported permanent recovery in 239 of these cases.

THE RELATION OF THE COMMON BILE DUCT TO THE PANCREAS

We shall not describe in detail the blood supply to the pancreas or its lymphatic structures, yet we think emphasis should be placed on the probable connection between the lymphatic structures of the gall bladder and of the pancreas and on that between the duodenum and the pancreas. Bartels stated that anastomosis can be demonstrated between these communicating lymphatics by injection either of one system or of the other.

The relation of the lower end of the common bile duct and the pancreas was accurately studied by Helly, who stated that either the lower end of the common bile duct lies in a niche of pancreatic tissue and that this niche is changed to a tunnel by the wall of the duodenum which is connected

with the common bile duct by fibrous connective tissue, or the common bile duct runs in a deep channel or through a tunnel made completely of pancreatic tissue. In a study of 58 cases, von Bunger found that in 55 the common bile duct passed through pancreatic tissue for a length of from 0.8 to 4.5 centimeters and that a layer of 0.2 to 2 centimeters of pancreatic tissue covered the common bile duct. These anatomic features make evident why a carcinoma of the head of the pancreas or marked inflammation of the pancreas will produce progressively increasing obstruction of the pancreatic portion of the common bile duct.

It is a fair assumption, we believe, that if a patient is jaundiced and there is dilatation of the extrahepatic passages and an indurated irregular tumor is palpable in the head of the pancreas, the lesion is probably carcinomatous. On the other hand, the incidence of pancreatitis as a possible cause of this obstruction forces the surgeon to be guarded in prognosis. The patient's progress over a period of time indicates the type of lesion which is producing the obstruction. The risk of removal of a portion of pancreas for microscopic examination at the time of operation on these deeply jaundiced patients, in our opinion, is not warranted.

SYMPTOMS

Carcinoma of the head of the pancreas occurs in later life. In this series, only 2 patients with carcinoma of the head of the pancreas were less than 40 years of age. One of these was a man of 34 years and the other a woman of 39 years. In 8 other cases in this series of patients who were younger than 40 years, the obstruction was due to an inflammatory process in the head of the pancreas. These obstructive lesions affected men twice as often as women.

Probably one of the most outstanding points in the differential diagnosis of tumors in the head of the pancreas has been the infrequency with which jaundice is associated with pain. In 99 of the 113 cases, the jaundice had painless onset. This, however, must not be taken to be a criterion of pancreatic obstruction of the common bile duct; in our experience the presence or absence of pain, with or without chills and fever, has depended more on the degree of the obstruction and the amount of infection in the biliary passages than on the factors which produced the obstruction, whether these factors were stones, strictures, or tumors of the head of the pancreas. This is exceedingly important, for by the same token that a patient with a stone in the common bile duct may have had painless jaundice, likewise a patient with pancreatic obstruction of the common bile duct may have had biliary colic either preceding the onset of the jaundice, such as occurred in 14 of our cases, or non-colic-like pain, such as occurred in 58 cases before or after onset of jaundice.

In a study, made in 1919, by Mussey, of 100 cases of carcinoma of the pancreas in which jaundice did not occur, pain was the predominating symptom. In cases of carcinoma of the head of the pancreas producing jaundice, pain may occur in the course of progress of the lesion. The correlation of the various types of pain with the observations at operation or at necropsy seemed to indicate that colic-like pain was associated with involvement of the ducts, that pain in the back was associated with involvement of the body and tail of the pancreas, and that pain in the left upper quadrant of the abdomen not infrequently occurred with diffuse, subacute pancreatitis.

Variations in the degree of jaundice, and the presence or absence of bile in the duodenal content, have afforded fairly accurate methods of determining whether the jaundice was intrahepatic, or whether it was due to obstructing lesions of the pancreatic portion of the duct. If a patient has painless jaundice and bile is obtained in the duodenal content by non-surgical duodenal drainage, by the Lyon tube, the jaundice is most likely to be of intrahepatic cause. When obstructing lesions in the head of the pancreas produce jaundice little bile is obtained in the duodenal content. Similarly, variations in the degree of jaundice, as well as variations in the amount of bile in the blood, as indicated by the van den Bergh test, have aided in differentiating the various types of biliary obstruction.

All distended gall bladders are not palpable through the abdominal wall. In a study by Weir and Partch of 275 cases in which operation was performed at The Mayo Clinic for lesions of the pancreas producing obstructive jaundice, a palpable gall bladder was noted in approximately 60 per cent of the cases.

Rapid loss of weight in cases of carcinoma of the head of the pancreas is a striking feature. In 54 of our cases the patients lost from 15 to 65 pounds (6.8 to 29.5 kilograms). As might be expected, gastro-intestinal symptoms, dyspepsia, anorexia, various types of indigestion, and in some cases vomiting, particularly in cases in which the lesion is advanced and produces extragastric or extraduodenal obstruction, are not uncommon. If duodenal or gastric obstruction occurs, and the condition of the patient permits,

we have not hesitated to perform gastro-enterostomy.

SURGICAL TREATMENT OF OBSTRUCTIVE JAUNDICE DUE TO PANCREATIC LESIONS

Much has been written before of the value of cholecystectomy and drainage of the biliary passages if a mild degree of pancreatitis has existed secondary to definite evidence of cholecystitis. The cases which we are studying and are presenting are those in which little, if any, evidence of infection is present in the walls of the gall bladder or the common bile duct, in which distention of all of the extrahepatic ducts is marked and in which evident thickening of the head of the pancreas seems to indicate the site of obstruction. In these cases cholecystenterostomy has seemed indicated. The benefits of operation in such cases have not only been relief of the jaundice and the troublesome itching, of which many of these patients complain so bitterly, but it has been the means of enabling thorough and certain exploration of the biliary passages, to eliminate the possibility of the presence of removable obstruction, such as stones.

The risk of cholecystenterostomy (13) has been due to two factors: the tendency to bleed as the result of severe jaundice, and renal and hepatic insufficiency subsequent to operation. It has been our custom to prepare for operation all patients with jaundice by a method which Walters described in 1921. The patients receive three daily intravenous injections of 5 cubic centimeters of a 10 per cent solution of calcium chloride. This may be diluted by adding 100 cubic centimeters of physiologic solution of sodium chloride. They are also given a diet high in carbohydrates, which often is supplemented by intravenous injection of glucose, 10 per cent, in physiologic solution of sodium chloride.

Whether the stomach or the duodenum is chosen as the site for anastomosis with the distended gall bladder is dependent on the accessibility of the structures and the ease of their approximation without tension. One should not hesitate to perform anastomosis of the gall bladder and the stomach in any of these cases, for apparently the presence of bile in the stomach is not a source of permanent discomfort.

The operation may be done in one stage or in two stages; the anastomosis may be made by suture or by use of a Murphy button. Decision as to whether the anastomosis should be done in one stage or whether cholecystostomy should be performed 12 or 14 days before the anastomosis, depends largely on the patient's condition. If jaundice is not too deep and the patient's general condition is satisfactory, there is no reason why cholecystenterostomy in one stage should not be carried out. In doing this operation in one stage one must be certain that there is no bleeding from the edges of the anastomosis and in this respect the use of a hæmostatic, inverting stitch, of the buttonhole locking type, serves admirably. If the jaundice is deep and the patient's condition is less satisfactory than is desirable, the jaundice can be diminished by preliminary cholecystostomy before the anastomosis is made. This not only decreases the jaundice and the tendency to bleed but also lessens the chance of precipitating hepatic and renal insufficiency. Walters, Greene, and Fredrickson have demonstrated that following cholecystostomy for relief of obstruction of the pancreatic portion of the common bile duct, a tremendous amount of fluid, as well as of sodium chloride, is discharged through the biliary tract and is lost from the body. If this loss is allowed to continue, in many instances, the patient will succumb from dehydration toxæmia in a comparatively short time. For this reason, the anastomosis between the gall bladder and the stomach or duodenum should be made approximately on the twelfth or fourteenth day following cholecystostomy, to prevent the occurrence of this dehydration toxæmia.

RESULTS OF OPERATION

Fifteen per cent of the patients in this series have lived more than 5 years, 25 per cent have lived longer than 3 years, one patient is living and well 13 years after operation, another died 13 years after operation from intercurrent disease, and 2 died 8 and 9 years respectively following operation. Twenty-four of the 113 patients were alive at the time they were traced. In 5 cases duodenal involvement or obstruction occurred. Four patients gained considerable weight after operation.

The question has arisen as to whether cholecystenterostomy, with the consequent loss of sphincteric action between the biliary and gastro-intestinal tracts, might not be followed by ascending infection of the intrahepatic biliary passages. Experimental work by Gatewood and Poppens, and by Beaver, suggests that such infection following cholecystenterostomy performed on animals usually occurs. However, clinical experience in man has not often corresponded with these observations. After study of the literature, Wangensteen stated that the complication of cholangitis following cholecystenterostomy has but infrequently been observed, and

that narrowing or partial occlusion of the stoma of the anastomosis, such as occurred in the case he reported, was the determining factor.

Our experience gives further confirmation to this statement. In 3 of the cases in which necropsy was performed, cholangitis and formation of abscesses had occurred. In all 3 cases, cholecystenterostomy had inadequately relieved the obstruction. In 2 cases, the cystic duct was invaded and obstructed by the tumor, and in 1 case the tumor of the cystic duct with the common bile duct was so low that the cystic duct was compressed and obstructed by the tumor at the head of the pancreas. Besides, one of our cases illustrated very well that cholecystenterostomy without obstruction is well able to take care of an infection of the biliary tract. One man had recurrence of jaundice, associated with chills and fever, 6 months after operation. This man returned to the clinic 6 years later, for treatment of chronic seminal vesiculitis; he had not had any gastro-intestinal trouble for many years.

The risk of operation in these cases is dependent on the condition of the patient, particularly on the duration of jaundice. The results of operations performed on the gall bladder and biliary passages at The Mayo Clinic in 1929 were reviewed by Judd and Walters; they found that in that year cholecystenterostomy had been performed in 10 cases for tumors in the head of the pancreas, without a death. In 1930 a similar number was performed with 1 death and that from bronchopneumonia. In this group, in more than half of the cases, jaundice was so deep at the time of operation that cholecystenterostomy was performed in two stages.

NATURE OF PATHOLOGICAL LESIONS AT THE HEAD OF THE PANCREAS PRODUCING JAUNDICE

Postmortem examinations in 26 cases in which there were tumors in the head of the pancreas which had produced obstructive jaundice, have shown that in 21 of the cases, the lesion was malignant: adenocarcinoma, scirrhous carcinoma, or mucus-cell carcinoma. Some of these 26 patients were in such poor condition that operation could not be performed. In 5 cases the obstruction was due to inflammatory lesions. Of the 21 carcinomata, 14 originated from the head of the pancreas; 4 from the lower end of the common bile duct, and 3 from the ampulla. Metastasis to the regional lymph nodes or to the liver was present in less than half of the cases.

Some cases in this series called attention to the fact that distention of the bile ducts and of the gall bladder, accompanied by a marked degree of biliary cirrhosis, may be found after a very short period of jaundice. A possible explanation for this was seen in a case in which gastro-enterostomy was done for duodenal obstruction due to carcinoma at the head of the pancreas. Jaundice had not occurred in this case. At operation marked distention of the gall bladder and bile ducts was noticed which may have existed for a considerable length of time. Seventeen days after the operation, jaundice developed. This was relieved by cholecystenterostomy. After recovery from the operation, the patient died of general carcinomatosis.

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BASAL CELL CARCINOMA OF THE VULVA[1]

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BASAL cell carcinoma may be defined as a special type of epidermoid tumor which has its origin in the basal layer of the epidermis, the sweat or sebaceous glands or the hair follicles. It has a characteristic clinical course and structurally has a specific gross and microscopic appearance. Since Krompecher's monograph in 1903 this tumor has been generally recognized as a definite pathological entity.

Typically, basal cell carcinoma adopts as its site of election the face. It occurs chiefly on the cheeks, nose or outer or inner canthi of the eyes. In a series of 268 cases reported by Broders, 96 per cent of the tumors were found above the clavicles. Schreiner, Simpson, and Mueller in a group of 59 patients reported by them stated that about 90 per cent of the lesions of their patients appeared on the face, all notably above a line drawn on a level with the upper lip.

In reviewing the literature concerning tumors of the vulva, one is immediately confronted with the loose use of terminology which makes for not a little confusion and misunderstanding. Taussig, referring to the existing confusion says, "a good illustration of this is to be found in the peculiar chronic infectious enlargement of the vulva to which the terms elephantiasis, pseudoelephantiasis, esthiomene, rodent ulcer, lupus, granuloma, and syphiloma of the vulva have been applied." Rather numerous cases have been reported under the title of rodent ulcer of the vulva which, on careful analysis, appear to be entirely chronic inflammatory lesions to which the authors have attributed various etiological factors, i.e., syphilis, gonorrhœa and tuberculosis. The cases reported as rodent ulcers by F. Jess, A. Rieck, O. Orsini and L. Machado, and M. Maffett are apparently of this nature.

We have been able to find only 2 instances in which basal cell carcinoma of the vulva has been described in the literature. In 1926, N. Temesváry reported the case of a 53 year old woman who had had recurrent erysipelas and furunculosis of the vulva. At the time of his examination she had multiple small nodules over the labia majora, the previous infection having subsided. None of these tumors was ulcerated. There was some œdema of the clitoris, labium minora, and inner aspects of the thigh but no evidence of tumorous involvement in those regions. Laboratory studies, including examination of the blood and urine, showed nothing unusual. The Wassermann reaction was negative. A biopsy from one of the nodules presented, on microscopic examination, a typical picture of basal cell carcinoma. The patient received radium treatment twice during the course of a month with no apparent change in the gross pathological picture. She then went to another clinic and died 4 months later from congestive heart failure.

V. Leigheb, in 1927, described the case of a 68 year old woman who, for about a year, had had an intense itching and prickling sensation of the vulva. She had had no previous treatment. On examination, both labia majora and minora showed some thickening with areas of ulceration and leucoplakia. The inguinal nodes were enlarged, firm, but not tender. The Wassermann reaction was negative. A biopsy was done and subsequently a vulvectomy with dissection of the inguinal nodes. From the microscopic studies, a diagnosis of basal cell carcinoma was made. The inguinal nodes showed no evidence of neoplastic invasion. Seven days following the second operation the patient died from bronchopneumonia.

We wish to present a case of basal cell carcinoma of the vulva which we have had the opportunity of studying. For this privilege we owe our thanks to Dr. F. W. Roberts of New Haven, Connecticut.

The patient, a white woman, aged 69 years, presented herself for treatment on November 3, 1930. Her complaint was a growth on the vulva and pruritus. She gave an interesting history. For the past 34 years, since the birth of her last baby, she had experienced a "deep itching, crawling" sensation on the left side of her vulva. For the past 6 years there had been present a small "growth" which had slowly increased in size. Occasionally it cracked open superficially and bled slightly. For many years dilute solutions of carbolic acid had been used to relieve the pruritus. This treatment was quite satisfactory for a time but had gradually become less effective. During the past few years various remedies had been tried which gave little or no relief. The menstrual history was essentially normal. The menopause had occurred at the age of 50. There was no history of venereal diseases. The patient had had three pregnancies, one miscarriage at 3 months' gestation and two normal spontaneous deliveries with children living and well now 36 and 34 years of age, respectively.

Her past history was of particular interest. On June 14, 1928, 2½ years previous to the present admission, she had entered the New Haven Hospital with the complaint of a gastro-intestinal disturbance. From the history, physical findings, and roentgenograms a diagnosis of carcinoma of the lesser curvature of the stomach was made. Examination of the genitalia at that time revealed a small, slightly

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reddened abrasion of the medial portion of the left labium majus. The Wassermann reaction was negative. At operation a partial gastrectomy with gastrojejunostomy was done. The patient made an uneventful convalescence and was discharged July 18, 1928, improved. The pathological examination of the tissue removed revealed an adenocarcinoma of the stomach with metastases to the regional lymph nodes.

At the present admission there was no evidence of gastrointestinal disturbance. The physical examination, except for the vulva and extremities, was essentially negative. No abdominal masses were felt. The lower extremities showed rather marked varicosities. Examination of the external genitalia revealed a relaxed outlet from which there was no discharge. In the midportion of the inner aspect of the left labium majus there was an irregular elliptical shaped area measuring about 3 by 2.5 centimeters in diameter. Superficially this was clearly demarcated and slightly raised above the level of the surrounding skin. Throughout, there were numerous small, shallow, ulcerated areas which appeared moist. To palpation the tumor was slightly indurated. It was not tender to pressure. There were no palpable inguinal lymph nodes. The laboratory findings were within normal limits. A clinical diagnosis of basal cell carcinoma of the vulva was made.

On November 4, 1930, using local anæsthesia, novocain infiltration, the tumor was excised and the resulting wound approximated without difficulty. No postoperative complications occurred and the patient was discharged November 8, 1930. At a follow-up examination on January 7, 1931, the wound was found to be well healed. The patient was entirely relieved of her symptoms. At a subsequent examination done May 1, 1931, there was found no evidence of recurrence. The patient's condition was satisfactory.

Pathologic study. Gross. The specimen consisted of an elliptical shaped piece of tissue which measured 3 by 2.5 by 0.6 centimeters. It was covered on the outer surface by epithelium, the borders of which were of a light brown color. The central portion, which was slightly elevated, presented a lighter colored area measuring about 2 centimeters in its greatest diameter. In this portion of the tissue there were several shallow ulcerated areas of varying size, the largest of which measured 1.5 centimeters and the smallest 0.1 centimeter in greatest diameters. The edges of these ulcerated areas were slightly elevated, firm, sharply defined, and irregular in contour. The bases were smooth, shallow, and pink in appearance. The inner surface of the specimen was covered by normal appearing fibrous and adipose tissue. On section the tissue offered little resistance. The cut surface presented a gray appearance throughout which lighter gray areas were seen which extended downward a short distance from the thickened epithelium and the ulcer beds, as irregular nodules and fingerlike projections. The ulcerated areas appeared to involve only the epithelial surface.

Fig. 1. Photograph of surgical specimen showing tumor and surrounding skin. Throughout the tumor surface the ulcerated areas are clearly shown.

Microscopic. The material was fixed in a neutral solution of formaldehyde (4 per cent). Some of the preparations were stained with hematoxylin eosin. Others were stained according to Mallory's technique for connective tissue and McCallum's and Ziehl-Neelson's methods for bacteria. The microscopic preparations showed one surface to be partially covered by stratified squamous epithelium. Throughout were seen several ulcerated areas limited by

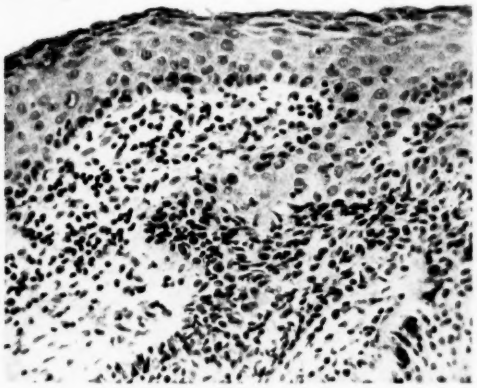

Fig. 2. Photomicrograph showing direct connection between the tumor cells and the rete pegs of the overlying skin. Hematoxylin eosin. ×220.

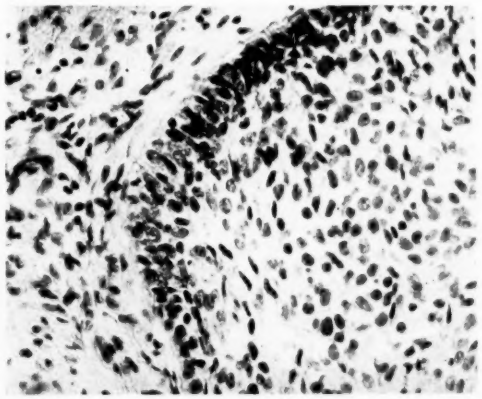

Fig. 3. Photomicrograph showing the smaller peripheral cells and the larger central cells. The hyaline-like connective tissue immediately surrounding the tumor is not shown as well as in the microscopic preparation. A few small round cells are seen in the surrounding connective tissue. Hematoxylin eosin. ×335.

sharply defined epithelial edges. Extending from the surface of these ulcerated areas for a short distance into the subcutaneous tissue were found strands and clusters of epithelial cells surrounded by rather dense hyaline-like connective tissue. The peripheral portions of these epithelial masses were composed of small cells varying in shape from cylindrical to spindle form, with scant cytoplasm and small darkly staining nuclei. The cells in the central portions were somewhat larger, more polygonal in shape, with clear staining cytoplasm and rather large nuclei, some of which were compact and others slightly vesicular. Similar masses of cells were found beneath the intact epithelium and in places they were connected with the overlying rete pegs. A few of the larger cell masses contained small cyst-like structures filled with a lightly staining granular material. In the connective tissue beneath the ulcerated areas as well as around some of the cell masses was seen a moderate cellular infiltration consisting of plasma cells and lymphocytes. A careful search was made for bacteria in the sections prepared with the appropriate stains but none was found.

Pathologic diagnosis: basal cell carcinoma.

Basal cell carcinoma of the vulva is exceedingly rare but probably more frequent than the specific literature would lead one to believe. In 1903 Krompecher described a case of basal cell carcinoma of the vagina occurring in a woman past the menopause. Basal cell carcinoma in general occurs in patients past middle life. In the 2 cases reviewed and our own case, the ages were 53, 68, and 69 years, respectively. In the case described by V. Leigheb as well as ours, pruritus was the predominant symptom. In the case of N. Temesváry, the preceding conditions were recurring attacks of erysipelas and furunculosis. Chronic irritation probably is as significant an etiological factor in this location as elsewhere. Long continued irritation according to H. Dittrick also acts as an important etiological factor in the formation of squamous cell carcinoma of the vulva. Pruritus is the most common symptom in this condition as well as in basal cell carcinoma.

N. Temesváry, in the treatment of his case, employed radium but was unable to complete the course of treatment because the patient moved to another clinic, hence he could not determine the value of this type of therapy. A vulvectomy with dissection of the inguinal nodes was done on the case described by V. Leigheb. There seems to be no justification for such a radical procedure. This case died a week later from bronchopneumonia. In our case a local excision was done and to date the patient has shown no evidence of recurrence.

CONCLUSIONS

1. Basal cell carcinoma of the vulva, though rare, does occur.
2. The clinical course and pathological picture are comparable to basal cell carcinoma occurring elsewhere, and the treatment should be the same.

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A NEW METHOD OF TREATING BREAST ABSCESSES

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IN presenting this paper it is not my purpose to review the different methods of treating breast abscesses. I wish to illustrate and describe briefly a method which has proved to be very satisfactory.

It is not necessary to enter into a discussion as to the etiology and prophylaxis of breast abscesses. Everyone is aware that prevention is important and practically all cases of breast abscess can be prevented, but due to the lack of knowledge or negligence of the attending physician or more often the mother, breast abscesses still occur too frequently during the lactation period.

The same principles are maintained in treating breast abscesses as in treating suppuration elsewhere in the body, that is, incision and adequate drainage, rest, proper elimination, and symptomatic treatment. The optimum time for incision occurs when definite fluctuation appears. Delay may mean extension and undermining of tissue with destruction of most of the lobules. In order to establish proper drainage by the usual method, it is necessary to make a large incision and oftentimes counter drainage is necessary. If it were possible to establish proper drainage with a small incision in the breast tissue, the ugly scarring could be avoided and normal breast tissue saved. DeLee states, "In opening abscesses some respect should be paid to the appearance of the breast."

Another important factor in treating breast abscesses is the question of dressings. If one has to pack open an abscess cavity with rubber tissue, gauze, or whatever seems suitable to use, the pack has to be renewed daily, causing severe pain unless an anæsthetic is used and one does not like to anæsthetize his patient for a change of dressings. On the other hand if the patient is not narcotized one cannot pack the cavity thoroughly.

The third point for consideration is a satisfactory support for the breast, that is, one which will lift the breast and give moderate compression and maintain that support from one dressing until the next.

It seems logical, therefore, that if one can overcome or minimize these three obstacles, one has made some progress in satisfactorily treating breast abscesses. The method about to be described aims to eliminate these difficulties, and experience has verified its practicability.

Adequate drainage through a very small incision can be established as follows: Under nitrous oxide anæsthesia, a stab wound is made large enough to accommodate a rubber tube, ½ inch in diameter. The incision should be made at the lower or outer margin of the abscess and carried radially from the nipple, staying outside the areola in order not to cut any of the lactiferous ducts. The finger is inserted into the cavity and all septa between the pus pockets broken down. The rubber tube, ½ inch in diameter, is then inserted into the cavity and fixed to the skin with a silk or catgut suture. A Dakin's tube is then inserted through the rubber tubing, or, if the cavity is large enough, two Dakin's tubes may be inserted (Fig. 1). The cavity may be thoroughly washed out with hypochlorite of sodium, a painless procedure. There can be no distention of the cavity with fluid for the large tube acts as a reflux. Carrel and Dakin introduced hypochlorite

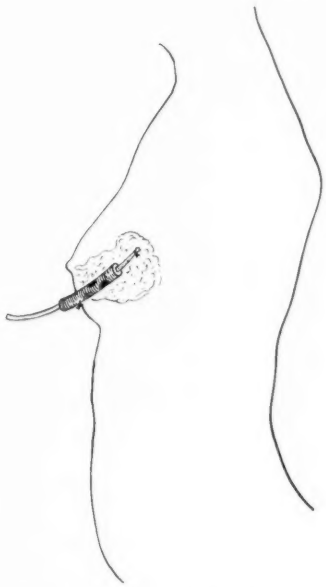

Fig. 1. Drawing showing a half-inch rubber drain inserted into the abscess cavity and anchored to the skin with a silk or catgut suture. A Dakin's tube is inserted through the rubber drain into the abscess cavity.

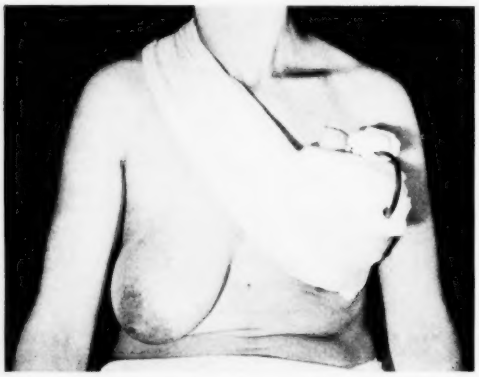

Fig. 2. A photograph of a patient showing the first procedure in applying the gauze roll bandage. Note the elevation of the breast in comparison to the opposite one.

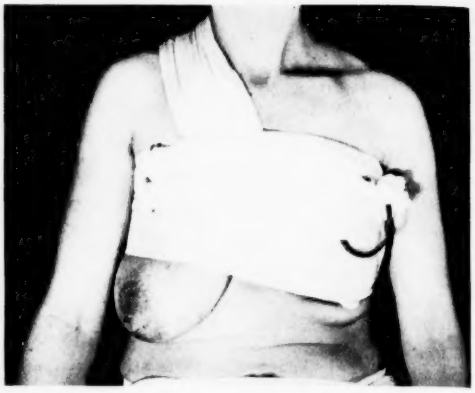

Fig. 3. Photograph showing the bandage completely applied. By carrying the bandage around the chest wall as much pressure can be applied as desired. Note the Dakin's tube brought out through the dressing, the end being kept sterile by placing a small piece of gauze over it.

of sodium during the World War as a means of treating infected wounds. The Carrel-Dakin method of treating empyema was adopted by the Empyema Commission, and has been of inestimable value. To my knowledge Dakin's solution has never been used in treating breast abscesses, at least, I have been unable to find it described in the literature. Dakin's solution is not only a disinfectant, but destroys certain unorganized fibrinous deposits; stimulates clean granulation tissue, and is a deodorant. It is important to introduce some solution which will destroy bacteria quickly, remove necrotic material, and not injure healthy tissue. One should incise the abscess as soon as fluctuation occurs and disinfect the cavity, thereby eliminating or minimizing the possibility of auto-infection and multiple abscess formation. Bacterial counts before and after the use of Dakin's solution give conclusive evidence of its bactericidal properties. The bactericidal properties of Dakin's solution have been affirmed many times in treating empyema cases. Within 24 hours the discharge changes from a purulent material to a seropurulent exudate. It stimulates healthy red granulation tissue. The tube can be left in until the wound begins to granulate around it. The Dakin's tubes can be brought outside through the dressing and the cavity irrigated without disturbing the dressing. If the patient is a hospital case, one can irrigate the cavity twice a day, if ambulatory, once a day will be sufficient. As soon as the cavity becomes collapsed and clean, the irrigations may be stopped. It is easy to measure the amount of fluid the cavity will hold, which is a good index as to the rapidity of the healing process. There is one warning about using hypochlorite of sodium, namely, it is irritating to the skin. The skin must be protected and the most convenient form of protection is vaseline gauze. (Vaseline gauze is prepared by cutting six-inch strips of gauze bandage, placing in a porcelain container with a large amount of vaseline on top, and sterilizing in the autoclave.)

Obviously one cannot insert a drainage tube into a small superficial subareolar abscess. A small gutta percha drain should be inserted at the time of incision and the cavity irrigated by placing a small piece of Dakin's tubing on the tip of the syringe and inserting into the cavity. Very gentle pressure should be used. One or two irrigations are usually all that is necessary.

As a dressing, vaseline gauze is excellent for any suppurating wound even though sodium hypochlorite is not used. It protects the skin from the irritating and macerating effect of the discharge, thereby preventing other avenues of infection, and the patient feels more comfortable. A very great advantage is that it can be removed from the wound without causing any pain, and it does not become adherent to the edges of the wound and skin. One can cover the vaseline with gauze flats or fluffs.

The question of supportive binders is one of importance. The requisites of a good binder are first, that it must lift the breast; second, that it must compress the breast against the chest wall; third, that it must not be too bulky and maintain its original application from one dressing until the next. Most breast binders become loose

and do not elevate the breast. Adhesive strapping gives good support and compression if long and wide strips are used, but adhesive tape is painful to remove, and many skins are sensitive to it, and a marked local reaction is produced. A satisfactory binder can be made of gauze 16 inches wide and 5 yards long, folded so that it is 4 inches wide. This can be rolled, wrapped in a cloth, autoclaved, and kept sterile. With the gauze roll, the mammary gland can be lifted upward by carrying the bandage up over the opposite shoulder (Fig. 2), and firm pressure can be secured by carrying the bandage around the chest wall (Fig. 3). These binders do not slip and in addition they serve as a protective dressing. When support is no longer needed and the drainage is scant, a small dressing applied with narrow strips of adhesive tape is substituted.

SUMMARY

1. The occurrence of breast abscesses can be prevented in great part by suitable prophylactic measures, but due to neglect by the attending physician or mother, breast abscesses still occur frequently during the lactation period.

2. It is important to establish proper drainage with minimum scarring of the breast. This can be done by making a stab wound large enough to accommodate a rubber tube ½ inch in diameter, which is made secure by suturing to the skin. Other drains and counter drainage will be unnecessary. A Dakin tube is inserted through the drainage tube and the cavity is irrigated with hypochlorite of sodium, which is a disinfectant, destroyer of necrotic material, stimulator of granulation tissue, and a deodorant. It does not harm healthy tissue.

3. Vaseline gauze is a dressing which can be removed and applied without pain to the patient. It protects the skin from the irritating and macerating effect of the discharge. It is imperative that this or some other oily dressing be used when the cavity is irrigated with hypochlorite of sodium.

4. A gauze roll makes an excellent binder, for it gives support, compression, and serves as a protective dressing.

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A MODIFICATION OF THE KIMPTON–BROWN METHOD OF WHOLE BLOOD TRANSFUSION

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THE practical value of the following modification of the Kimpton-Brown method of whole blood transfusion warrants its publication.

Apparatus. Glass tubes of 300 cubic centimeters capacity, special needles with obturators, and a rubber, pressure-suction bulb, constitute the apparatus. The tips of the glass tubes are similar to the tips of the large Luer syringes. The needles are Nos. 14 and 16 for donor and recipient, respectively, and are equipped with obturators which mechanically fill the hub and barrel of the needle, similar to obturators of lumbar puncture needles (Fig. 1).

Preparation of apparatus. With the cork stopper removed, the tubes are thoroughly cleaned and dried. A cubic inch of solid paraffin is placed in each tube, the cork inserted in the upper end and tied securely by means of a string which passes over the cork and around the glass tube below the airway (Fig. 2). Several such tubes are prepared in this manner and are placed in the autoclave for sterilization. With gloved hands and a sterile towel, the tubes are gently rolled, while the paraffin is still liquid, a small amount of paraffin being allowed to escape through the tip and to coat the entire inner surface of the tube. The tubes are then placed with the upper end downward, and the excess paraffin is alowed to accumulate and solidify next to the cork above the airway. This will prevent air escaping around the cork when the blood is being injected. The tube is then wrapped separately in two sterile towels, which are held in place by rubber bands, and stored away until needed. In rural districts, the oven of a cooking stove may be used instead of an autoclave. It is not necessary to sterilize the rubber bulbs.

The needles should be sharpened on a fine emery and oil-stone disc 4½ inches in diameter, propelled by a small hand motor, obtainable from any hardware store. The hollow ground effect imparted to the needle by these disc stones is of definite advantage in entering a vein. The proper length of the bevel of a needle for intravenous use is one and one-half times the diameter of the needle. The needle should be sharpened by the person who intends to use it and sterilized by lysol or by methods usually used in sterilizing sharp instruments, and not by boiling or by the autoclave, as the latter would interfere with the needle's holding a sharp edge because of change in the temper of the metal. After sterilization the needles should be thoroughly dried with ether and placed in separate test tubes with a pledget of cotton at the bottom, which is saturated with liquid petrolagar. Needles thus cared for will not rust and can be prepared and kept for use at any time.

Procedure. A No. 16 needle is inserted into the vein of the recipient and plugged with the proper obturator which, because it completely fills the hub and lumen of the needle, prevents the loss of blood and, equally important, the formation of a clot in the needle. A No. 14 needle and a suction bulb are attached to a paraffin coated tube (Fig. 1). This needle with the tube attached is inserted, point toward heart, in the vein at the elbow of the donor. With a blood pressure apparatus applied as a tourniquet at an optimum pressure of 30 millimeters of mercury and with a vacuum created in the tube by means of the suction bulb, 250 cubic centimeters of blood is collected in an average time of about 60 seconds. The tourniquet is released and the paraffin tube is disconnected from the donor's needle, which is immediately plugged by the proper obturator and left in the vein of the donor.

The suction-pressure bulb is reversed. The paraffin tube is connected with the needle in the recipient's vein and the blood is injected as rapidly, or as slowly, as desired. More than one bulb must be at hand so that in case a valve of one fails to act, another can be quickly substituted. If the needle in the patient's vein should happen to get dislodged after the blood has been collected from the donor, the blood should be reinjected into the donor's vein until the needle is replaced into the patient's vein. *The pressure bulb must be released just before the last 5 cubic centimeters of blood is injected, to prevent air entering the vein.* With another paraffin coated tube, 250 cubic centimeters more blood is collected from the donor and introduced into the recipient. This can be repeated if necessary, until the desired amount of blood is transfused. Four tubes of blood have been taken from a vein of one donor at one sitting.

If the patient is an infant or has collapsed veins, a vein is exposed by a skin incision, under

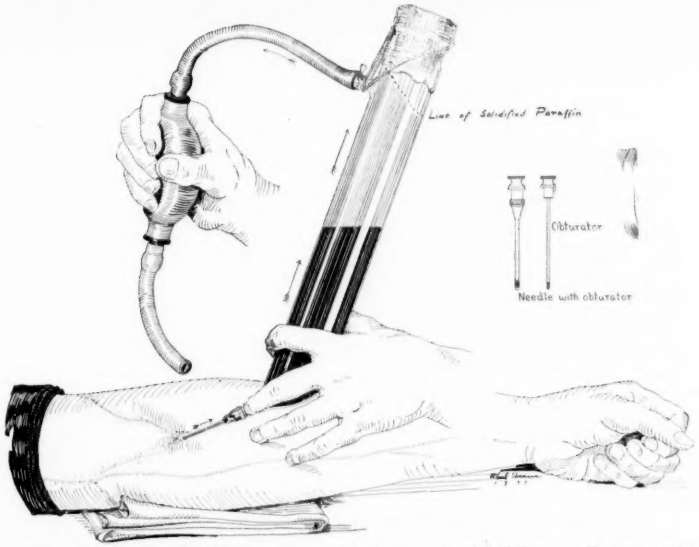

Fig. 1. Collecting blood from donor. Note manner of holding needle onto tube with middle finger. Also note that fourth and fifth fingers rest on forearm of donor to steady needle in vein.

MIDDLE FINGER HOLDS NEEDLE
THIRD AND FOURTH FINGERS REST ON PATIENT
PRESSURE MUST BE RELEASED WHEN BLOOD IS AT THIS LEVEL

Fig. 2. Pressure bulb must be released at point indicated to prevent air embolism.

local anæsthesia, and opened by a tangential incision and a dulled needle inserted and tied in. In newborn babies or small children, the internal saphenous vein over the internal malleolus is *always* present and of ample size.

The author, within the last 10 years, has done over 1,200 blood transfusions by this method, with but one failure. In this instance, an Italian donor, husband of the patient, fainted, and blood could not be obtained from him by any method after his veins were exposed and incised. In this series there have been 7 reactions accompanied by a hæmoglobinuria, 12 chills with moderate fever, and one immediate death in an infant, due presumably to giving too much blood, or an error in the laboratory tests. Both grouping and cross-agglutination tests are carefully performed by the microscopic method before any transfusion is given. The method has been adopted as a routine method by others in San Francisco, and many of my former house doctors have mastered the technique. To succeed consistently one must use sharp needles and enter the vein without undue trauma and without creating a hæmatoma, requirements of any needle method.

ADVANTAGES

The following advantages are claimed for the method:—

1. *Warm* whole blood is tranfused rapidly before precoagulation changes occur, thus preventing many reactions.

2. The blood does not come in contact with any rough surface, such as rubber tubing, thus the trauma to the blood is reduced to a minimum.

3. It is a one-man method thus eliminating the necessity for trained ones and the possible errors of untrained ones.

4. The patient and donor may be in different rooms if desired for psychic effect.

5. The possibility of infecting the donor from the patient is overcome.

6. No saline or other solution is required.

7. The necessity of cutting down upon the donor's veins is eliminated and only very rarely is it necessary to do so on the recipient. In one donor the same vein has been used by me 18 times and it is still good.

8. The method is rapid—an advantage in shocked patients. The procedure requires from 8 to 15 minutes' time.

9. A transfusion may be performed in a home, in a hospital room or ward, or in the operating room, without the necessity of scrubbing one's hands or wearing rubber gloves.

Paraffin tubes and needles may be obtained from the American Surgical Sales Corporation, on the Pacific Coast, or Messrs. Macalaster-Bicknell Company, Cambridge, Massachusetts.

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SPREADING PERITONITIS COMPLICATING APPENDICITIS

IN their literal interpretation few terms used by the surgeon vary as much as do general or diffuse peritonitis. These terms are used in an attempt to describe a process of unknown extent which cannot be determined accurately by physical examination or seen at operation. The term "local" is definite in its meaning. "General" or "diffuse" denotes the extension of the process to the entire peritoneum but "spreading" suggests an actively progressing process.

Frequently the diagnosis of a spreading peritonitis is made before operation because of the presence of extreme rigidity of the abdominal muscles. This rigidity is a reflex process running by way of the intercostal and lumbosacral nerves. However, the terminals of these nerves are irritated only when the parietal peritoneum is involved. The peritoneum covering the posterior abdominal wall may be involved without producing rigidity.

Many physicians emphasize the importance of distention as an aid in the diagnosis of spreading peritonitis but distention invariably occurs late and is therefore of no value in making an early diagnosis. Absence of peristalsis may be a significant factor in making a diagnosis, but in the early stages of a spreading peritonitis there may be intestinal contraction as evidenced by gurgling in segments adjacent to the site of the infection. Localized tenderness is an important early sign but frequently it is interpreted as the result of a lesion in an organ when actually the process has spread to the peritoneum. While rigidity and localized tenderness are the most important signs, in early peritonitis the former may be absent and the latter not marked if the appendix is abnormally located and the infection is spreading retrocæcally or toward the pelvis.

The diagnosis of a spreading peritonitis complicating appendicitis is most frequently made at operation. When a long vertical incision is made it is possible to determine the extent of peritoneal involvement but this method always involves danger to the patient. Dudgeon and Sargent in 1905 used this incision. Long vertical incisions, however, are not always used in operating for appendicitis. Of 3,095 patients operated upon in Philadelphia in 1930, by 338 surgeons, the McBurney, transverse or oblique incisions were used in 37.8 per cent. It is evident that the extent of peritonitis could not be determined by inspection in these cases. Furthermore, in some cases of spreading peritonitis but slight visible pathological changes are evident in the peritoneum.

The diagnosis of peritonitis complicating appendicitis is seldom made before the patient enters the hospital; for example: of the 8,216

cases admitted to 28 hospitals in Philadelphia during 1928, 1929, and 1930, the diagnosis of peritonitis was made in less than 10 per cent although peritonitis was a complication in 40.1 per cent of the cases; 14.2 per cent of the patients admitted had a spreading and 25.8 per cent a local peritonitis.

Every case of peritonitis recorded "local" on admission must have shown the symptoms and signs of a spreading process before admission. These symptoms and signs were sufficient to make a diagnosis only of the appendicitis and not of the peritonitis. It is evident, therefore, that, if proper management is to be instituted, more attention must be paid to the reaction of the patient to the infection. Physical signs are important but a careful history and an honest attempt to determine what nature's defensive mechanism is trying to accomplish is more important.

Acute fulminating appendicitis, developing within a few hours, characterized by suppuration and gangrene without perforation associated with high temperature and pulse rate is not the usual type of appendicitis, but even in this type the physical findings are usually those of a local process. The indications for operation are definite. A patient suffering with this type of infection, however, if given a laxative will, in most instances, suffer a perforation and the physical findings will vary with the location of the appendix; if retrocæcal or pelvic the perforation may be grossly sealed, the physical signs may be, and frequently are, those of a localized process, but the patient has actually a spreading peritonitis as evidenced by his reaction to the infection and if he is operated upon at this time before he has an opportunity to immunize himself against it he will probably die. Of every 8 patients 7 that were given laxatives and subsequently developed a spreading peritonitis died. Of those that were admitted to the hospital without a history of having taken a laxative during an acute attack 1 in 80 died; of those that took one laxative, 1 in 13 died, and of those that took two or more laxatives, 1 in 7 died.

To operate in the presence of a spreading peritonitis invites catastrophe. The day has passed when an intelligent surgeon interferes with nature in the localization of a skin or subcutaneous infection, by making incisions over lymph channels that are clearly delineated by their redness. The surgeon today gives the patient an opportunity to immunize himself against the infection and then, when temperature and pulse have subsided, the lymphangitis has disappeared, and the abscess well walled off, he makes a small opening in the center and inserts a drain. The management of general peritonitis is identical. We cannot see what takes place, what we feel is only a slight indication of the extent of the pathological process; how the patient reacts tells us a great deal more.

JOHN O. BOWER.

THE MULTISTAGE OPERATION IN TOXIC GOITER

THE ever broadening field of surgical therapy, the facility with which operations, scarcely conceived a generation or two ago, are now performed and the assurance with which formidable procedures upon vital organs are undertaken with every prospect of a successful outcome, have led, among other forms of technical improvement, to the development and increasing use of multistage operations. These methods, largely of recent origin, are exemplified by the procedures of a preliminary colostomy, or ileocolostomy, before resection of the colon; of suprapubic cystostomy in certain cases of prostatic hypertrophy; and of graded operations on the lungs, the œsophagus, and the brain. In no field of

surgery has the plan of the multistage, or divided operation, proved so valuable, and yet in no field has its utility been so widely debated, as in that dealing with treatment of diseases of the thyroid gland.

When the surgical treatment of goiter began to receive special attention, as was the case about 20 years ago, ligation of the superior thyroid arteries became an established and frequently utilized technique. In many clinics a majority of the patients with exophthalmic goiter received preliminary ligations; while certain surgeons refused to perform a thyroidectomy without this preliminary step. The operation was performed not so much as a means of reducing the technical difficulties of the major part of the treatment but rather as a test of operability, and, especially, as a means of improving the patient's general condition, thus reducing the risk incurred on the occasion of the subsequent thyroidectomy. The ligated patient improved as a result of a definite physiological effect produced within the gland itself not, as is sometimes the impression, merely as a result of the rest regimen simultaneously prescribed. Possibly, hundreds of these minor procedures were unnecessarily performed, yet it must also be true that many patients were saved who, without this preliminary step would have succumbed had they been subjected to a primary bilateral resection. In the same era the plan of multistage partial lobectomy was extensively followed. As our knowledge of thyroid physiology and pathology increased and as surgical technique improved, especially after the introduction of iodine in the patient's pre-operative preparation, multistage operations were less frequently performed until they almost disappeared from our operating lists. It became the fashion to place oneself in the position of saying that one never ligated, while, although it was not so universally discarded, the divided thyroidectomy also lost much of its former popularity, not because of any apparent lack of utility, but because, as if this implied technical simplicity were convincing evidence of our surgical progress, it had become the surgical style not to resort to it.

Desirable as lack of complexity in any surgical procedure may be, the definite value of these multistage operations, including superior pole ligations, should not be lost sight of. At present there seems to be a logical and fortunate swing-back to the occasional use of these procedures, the desirability of which has recently been referred to by Clute, who states that, as the percentage of operations per patient increases, the mortality percentage has decreased. If a hundred primary thyroidectomies are performed by surgeon A, who never resorts to other procedures, with no deaths following, but his one hundred first patient dies; while surgeon B performs one hundred and one thyroidectomies—a few being in stages —and all his patients recover, the question of which operator had the better results and, it may be supposed, exercised the greater judgment, can hardly be open to debate. The problem is the determination of what constitutes *too much* surgery in the individual case.

Although the use of iodine in the pre-operative preparation of the patient has greatly lessened the need for thyroid arterial ligation, the simplicity of the procedure and the startling improvement it almost invariably produces, render it too valuable a procedure, especially in the treatment of the extremely poor risk, to justify its present lack of unpopularity, the same being true of multistage thyroidectomy. The latter procedure, particularly with patients with long standing nodular, toxic goiter associated with serious cardiac disease, emaciation and marked weight loss, is of the utmost utility; and while deaths today rarely follow operation performed upon

the thyroid, the number which do occur can surely be decreased by more thorough study of the patient, more careful pre-operative preparation, and, most important, by exercising greater surgical judgment in adapting the type and extent of the operation to the individual patient.

Every surgeon interested in goiter is aware that many patients whose conditions seem perilous frequently recover promptly from formidable operations and with but little reaction; while others who are, apparently, extremely safe risks, occasionally succumb following the simplest of procedures. The greater his experience, the surer the surgeon becomes that he must ever be on the watch for the unexpected; must circumvent it if at all possible.

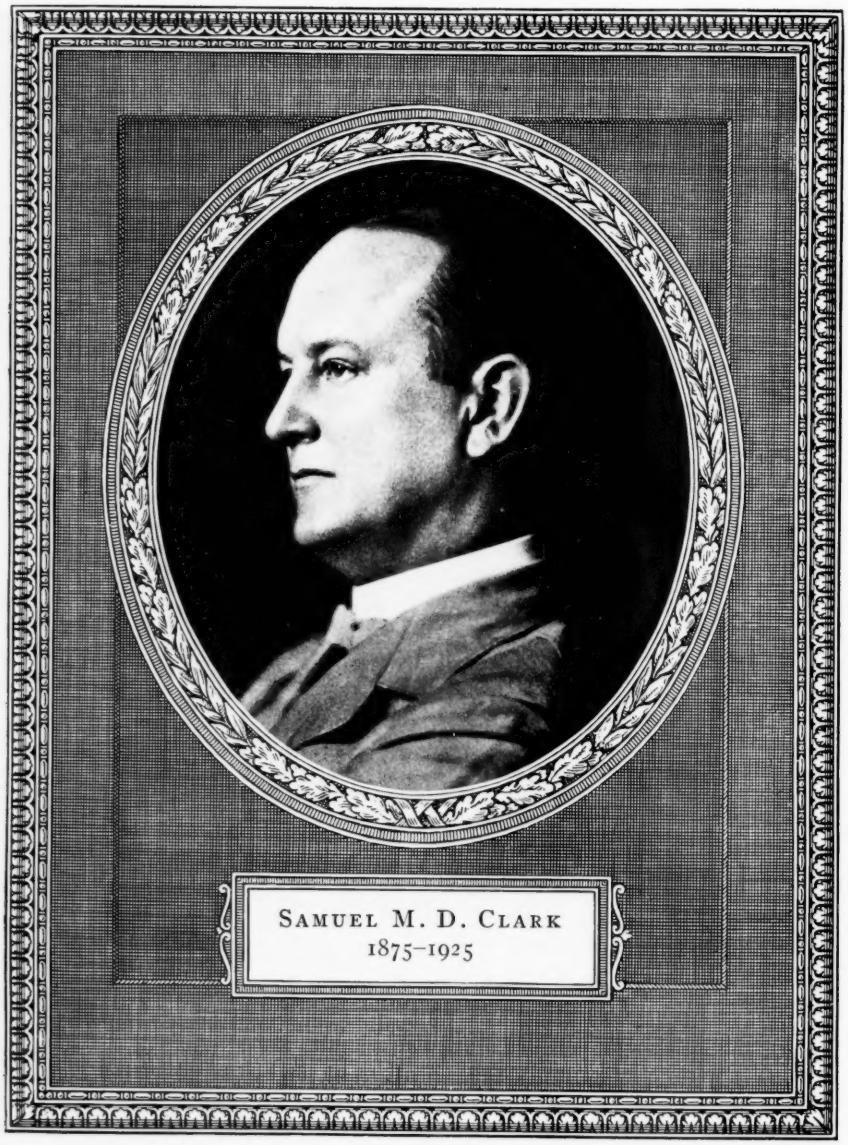
Death following primary thyroidectomy nearly always occurs with the patient who would not have succumbed had a divided operation been performed; but what patients to select for the procedure is a difficult problem, the parallel of which is not to be found in the treatment of any other surgical condition. It is realized that all patients can not be subjected to such a routine, but there are certain ones for whom the multistage operation is certainly indicated.

That one surgeon cites a long series of operations, performed in one stage, with little or no mortality, while the next, who occasionally utilizes the more conservative procedures alluded to, has a much higher death rate, proves nothing; neither does the fact that, in a given series, the only patients who died were those operated upon in stages. All the factors must be tabulated before an accurate comparative appraisal of end-results can be made and conclusions drawn, a principle which applies to all statistical analysis.

Pre-operatively administered Lugol's solution, as helpful as it definitely is, does not necessarily assure a successful outcome following a primary thyroidectomy. Prolonged, incorrect use of iodine has a real bearing on the results, a fact repeatedly emphasized, quite recently by Goetsch, who again stated that iodine should be employed solely in the preparation of the toxic patient for operation.

If any lesson is to be learned from all this, it is that one should not be greatly influenced by what may prove but a temporary vogue, to give up old and dependable friends, but should exercise certain individuality based on one's own experience provided, of course, it has been sufficiently extensive, and this applies, particularly, to the surgical treatment of toxic goiter where judgment of an especially high degree is demanded in properly fitting the operation to the individual patient.

HAROLD L. FOSS.



SAMUEL M. D. CLARK
1875–1925

MASTER SURGEONS OF AMERICA

SAMUEL M. D. CLARK

BY birth, inheritance, education, and lifelong residence in his native state, Samuel Marmaduke Dinwiddie Clark was a thorough Louisianian. He was born at Devall, West Baton Rouge, on his father's plantation, on July 28, 1875, and was approaching his fiftieth birthday when his career of great activity and usefulness was abruptly brought to a close by the fatal illness (diabetes, cardiovascular disease), which ended April 26, 1925.

Death came at a time when the splendid promise of his early years was being fulfilled and he was reaping the reward of a life of brilliant and constant service to his people, to his profession, and to the institutions with which he was connected.

His father was William Lobdell Clark, of Clarkland Plantation, Louisiana; his mother, Mary Elizabeth Devall, of Smithfield Plantation, West Baton Rouge Parish, Louisiana, and he inherited from each the qualities which were so distinctive of his character and personality. Like the sons of most planters of the last generation, his early education was entrusted to private tutors. He was graduated from the Louisiana State University in 1895 with the degree of B.Sc., after having been captain in the cadet corps during his senior year. In the fall of the same year he entered the School of Medicine of Tulane University and served as undergraduate interne at the Touro Infirmary in 1897. He was also an interne at the Charity Hospital from 1898 to 1900, and was graduated M.D., Tulane, in 1900.

In 1903, he was appointed assistant demonstrator of operative surgery under Professor Gessner in the Miles Laboratory of the Tulane School of Medicine. In 1904–1905 he was chief of clinic for Professor Lewis at the Charity Hospital, and in 1905 he was appointed lecturer and clinical instructor in gynecology and obstetrics. In the interim he was secretary of the Orleans Parish Medical Society and of the Charity Hospital Alumni Association of Louisiana. In 1907, he was elected assistant professor of gynecology in the School of Medicine under Professor Lewis. On the retirement of Professor Lewis, in 1911, his chair was divided, Dr. Clark succeeding him as full professor of gynecology and clinical obstetrics, and Dr. C. J. Miller, likewise, as professor of obstetrics and clinical gynecology. From 1911 to 1925, fourteen years, Dr. Clark served uninterruptedly as the effi-

cient head of the department of gynecology. Joined to his professorship in the medical school he taught and practiced at the Charity Hospital as visiting gynecologist of that institution and later became a member of the staff of Touro Infirmary in a similar capacity, continuing in both of these positions to the time of his death.

In addition to his active and conspicuous membership in the Orleans Parish, Louisiana State and American Medical Associations, Dr. Clark was a Fellow of the Southern Surgical Association (Vice-president, 1915), of the American Gynecological Society, the Southern Medical Association, and of the American College of Surgeons. In all of these he was a prominent figure, participating most actively in all their proceedings and contributing valuable papers and discussions.

During the World War, Dr. Clark was appointed Major in the Medical Corps and the first chairman of the medical section of the Council of National Defense in Louisiana. He was among the first surgeons to join the medical reserve corps and was assigned by the Surgeon-General to the special and important duty of inspecting the base hospitals in the cantonments. Selection for this delicate and difficult task was in recognition of his wise knowledge of operative surgery, hospital organization, and early training as a military cadet. When his tour of inspection had been completed he was again detailed for special duty overseas with the expeditionary forces in France, where he also rendered valuable service.

Dr. Clark found time amid his large professional interests to participate in the social life of the metropolis. He was a Mason, a member of the Boston Club, Audubon Golf Club, New Orleans Club, and Kappa Sigma and Phi Chi Fraternities, in all of which he was a prominent and highly esteemed member. He was passionately devoted to the outdoor life, and golf claimed his presence on the links whenever he could spare a moment to indulge in his favorite exercise.

In 1902, he married Miss Elise Cockerham, prominent in the social life of Natchitoches, who survives him. He is also survived by a sister, Mrs. Walker B. Spencer, and a brother, W. L. Clark, both of New Orleans.

Though not a voluminous writer, Dr. Clark contributed a number of very valuable and impressive papers to the medical press and to the *Transactions* of the societies of which he was a member. He wrote on subjects that especially interested him and which attest to his unusually clear and eminently practical judgment, his skill as an operator, his vigorous and progressive tendencies, and his broad learning in the literature of his profession. His papers on "Cesarean Section," "Treatment of Carcinoma of the Uterus," "Pelvic Infections," "Endometrial Transplantations," "Surgical Treatment of Visceroptosis," "Radium," etc., are merely cited among many other contributions to show his wide and varied interest in his specialty. He was always a ready, forceful, pleasing speaker in all matters that interested him or that concerned his province. The frequent invitations that he received to address the various parish and district medical societies

of Louisiana and of the surrounding states are proof of the merit and weight attached by his colleagues to his discussions and of the appreciation in which he was held by the profession throughout the country.

While intensely interested in his work and giving his best thought and energy to the discharge of his duties, whether in the classroom, at the operating table, or at the bedside, he was capable of the fullest relaxation and enjoyment of the amenities of life when the tension of his immediate task was over. Dr. Clark's popularity as a club man, with his students and in all social gatherings, in and out of the profession, is easily accounted for by his many lovable traits and genial characteristics. Physically endowed with a very attractive and approachable personality, he possessed an unusual inborn capacity for captivating friends and entwining himself in the affections, not only of his patients, of his students, and of his associates, but of all the men and women with whom he came in contact. Of graceful manner and speech, he was delightful as a *raconteur* and always a charming companion on any occasion. Though playful and wonderfully adaptable to any environment into which he might be thrown, he was none the less very firm and determined in his opinions and convictions. Though seemingly docile, even shy and unobtrusive, he was thoroughly conscious of his rights, and whenever these were trespassed, or he suspected that they were trifled with, he was sure to assert himself in a way that left no room for cavil or doubt. He was every inch a man, strong in his likes and dislikes. While he had long schooled himself to control his emotions and reactions, he was quite frank and always dependable in whichever direction he was led by his convictions. It was the charm of his personality and the virile quality so dominant in his composition which contributed largely to his popularity and to the tenacity and loyalty in which he held his friendships.

In closing this very inadequate sketch of Dr. Clark's distinguished career, reference should be made to the memorial resolutions adopted by the Faculty of the Medical School of Tulane University, which testify in feeling terms to the distinction that he gave to his department during the twenty-two years that he served and taught in his Alma Mater, to the affection in which he was held by his pupils and fellow workers, and to the great void caused in the school by his untimely loss.

RUDOLPH MATAS.

EARLY AMERICAN MEDICAL SCHOOLS

WILLAMETTE UNIVERSITY MEDICAL SCHOOL

O. LARSELL, PH.D., PORTLAND, OREGON
University of Oregon Medical School

THE third medical school to be founded west of St. Louis appears to have been that organized in Salem, Oregon, on February 15, 1865, by the Board of Trustees of Willamette University. In point of continuous existence, until it closed its doors in 1913, it was the oldest from the time of first organization, although Toland Medical College, now the University of California Medical School, began actual instruction somewhat earlier. It may also be noted that the medical department of the University of the Pacific, which later became Cooper Medical College, and is now continued as Stanford University Medical School, was founded in 1858, but discontinued in 1864, to be later resumed. The Oregon school was organized as the medical department of Willamette University. It was to be located at Portland under the name of "Oregon Medical College."

Willamette University was founded at Salem in 1842 by Jason Lee, the pioneer Methodist Episcopal missionary to the Oregon country. Lee and his associates had come to Christianize and teach the Indians, but the decimation of the Northwest tribes by the great epidemics which swept Oregon one hundred years ago and continued for a number of years so that the native population was greatly reduced, led Lee to turn his attention to the education of the children of the increasing white population. He founded the "Oregon Institute," with the definite aim of affording higher education to the white children of the Oregon country. The name was later changed to Willamette University.

In 1865, only 6 years after Oregon was admitted to statehood, another significant step was taken in the launching of a medical department. Governor A. C. Gibbs and others had taken the initial steps in 1864 by sending a communication to the Board of Trustees of Willamette University asking them to organize a medical department and to locate it at Portland. At the meeting of the Board the following February favorable action was taken. Provision was made by which the Board should appoint the medical faculty.

A faculty was elected and a temporary office of the school opened in Portland, but difficulties arose which resulted in temporary postponement of the project. The first faculty consisted of R. Glisan, M.D., professor of the theory and practice of medicine; J. A. Chapman, M.D., professor of civil and military surgery; A. M. Loryea, M.D., professor and demonstrator of anatomy; R. B. Wilson, M.D., professor of physiology and institutes of medicine; Hon. A. C. Gibbs, professor of medical jurisprudence; and Judge M. P. Deady, emeritus professor of medical jurisprudence. This faculty never gave instruction. It is interesting to note that an emeritus professor, the leading lawyer in the State, was included before the school began to function.

In June, 1866, steps were taken to bring the department into operation. This was apparently due in large part to the influence of Dr. J. H. Wythe, a physician, preacher, and educator, who became president of Willamette University in October, 1865. Since the medical department had failed to begin its work in Portland, it was proposed to locate it at Salem, with the other departments of the University. After some negotiations, through committees, with the previously named faculty, the latter "resigned their positions and discontinued their relations to the University." The Board voted on November 14, 1866, to establish the medical department at Salem. The following new faculty, consisting of physicians resident in and near Salem, was elected, namely: Horace Carpenter, M.D., professor of civil and military surgery; E. R. Fiske, M.D., professor of pathology and practice of medicine; John Boswell, M.D., professor of obstetrics and diseases of women and children; J. H. Wythe, M.D., professor of physiology, hygiene, and microscopy; D. Peyton, M.D., professor of materia medica and therapeutics; J. W. McAfee, M.D., professor of chemistry and toxicology; A. Sharples, M.D., professor of descriptive and surgical anatomy; W. C. Worimer, M.D., demonstrator of anatomy;

Hon. J. S. Smith, professor of medical jurisprudence. This was the first faculty actually to give medical instruction in the Pacific Northwest. Dr. H. Carpenter was elected dean.

The first course of lectures was begun on March 3, 1867, and at the Commencement of that year, W. A. Cusick, D. M. Jones, and J. L. Martin were graduated in Medicine. The second term was begun November 4, 1867, and continued 20 weeks. Attendance at two courses of lectures was required for graduation. The facilities for medical instruction in Salem were most meager. The entire equipment of the university, so called, consisted of one building, in which were lodged all departments, college, preparatory, and now, medical. There are references to a separate building for dissection, apparently a shed. The clinical facilities may be judged from the fact that the population of Salem at the time was about 1,200, and all of Marion County, in which Salem is located, had 7,000 people. However, as compared with many other medical schools, even in the older settlements of the East, the new department at Salem does not suffer too much. It was established in the belief "that the interests of the country would be promoted."

Horace Carpenter, M.D. (1826–1893). First dean of the Willamette Medical School.

While the faculty was appointed by the Board of Trustees of the university, the connection between the two bodies appears to have been more in name than in fact. Many misunderstandings arose, partly within the medical faculty itself, and partly from the inclination of many of the faculty to govern itself without reference to the Board. Within less than 2 years, a resolution was presented to the Board to discontinue the medical department. The resolution was tabled and the department continued in operation. Dissensions within the faculty continued, largely over the professorship of surgery, which "became a bone of contention and required all the patience and management . . . . to prevent an open rupture." The faculty reorganized, but there were several years of difficulty and disagreement. The story of these years is somewhat fragmentary, much of the record having been lost.

In 1870, it was proposed to donate ground belonging to the university for a hospital, but this plan was not carried out. Three years later the Board appropriated funds to rent quarters for the department in the town. Doctor Carpenter, who had been dean at various times, who continuously served as professor of surgery, and around whom many of the disagreements had arisen, resigned in 1875. Dr. D. Peyton was made dean for a time, and in 1876 twenty-three matriculants were registered in the department. Two years later, June 10, 1878, the Board of Trustees of the university voted to move the department to Portland, 55 miles away, where the initial attempt had been made 13 years earlier to establish it. Dr. O. P. S. Plummer, of Portland, was then made dean and a new faculty was appointed, although it included some who had served at Salem. Instruction in Portland formally began on December 16, 1878, but the first faculty meeting was held on June 18, 1878.

The school was housed in rented quarters and dissecting was done in some rooms above a livery stable for many years, although efforts were made from time to time to obtain more suitable quarters. It was not until 1887 that it moved into a building erected for purposes of medical instruction, which for its day was well designed and equipped. The funds for its erection, about twenty-five thousand dollars, were obtained from the Methodists of the state. It appears that perpetual scholarships were issued to contributors to the amount of five hundred dollars. This method of securing funds was used by other educational institutions during this period in the development of the state.

The motives which led to removal to Portland are not far to seek. In addition to the dissensions of the faculty at Salem, there remained the question of population. In 1878, Salem had about 2,500 people while Portland had grown to 19,128, and so provided more abundant facilities for instruction. Another factor appears to have been the activities of the Oregon State Medical Society, which was organized September 1, 1874. At its second meeting, the following year, an active interest in medical education was manifested in the appointment of a committee on medical education, with instructions to report annually on the general condition of medical education in the

state and on requirements for graduation, etc. Three years later a special committee was appointed to attend the examinations of the medical department of Willamette University, and the address of Dr. L. L. Rowland, president of the society in 1878, had for its topic, "Medical Education." There was a considerable interest in the subject on all sides.

However, a more immediate factor which led to moving the department was the organization in 1877 under the old name of "Oregon Medical College" of a proposed school in Portland, with several of the original faculty of 1865 on its list. The Willamette faculty was invited to appoint a committee to confer with a committee of the new school "to devise a plan, if possible, whereby the interest of both institutions may be so harmonized as to lead to the continuation of *one* medical college made capable of offering the most complete facilities of obtaining a medical education." As a result of the negotiations between the two committees, the Willamette faculty in June, 1878, recommended to the Board of Trustees of the university that the medical department be transferred to Portland "on the abandonment of the projected medical school there."

Building erected in 1887 for Willamette Medical School at Portland.

The Willamette medical department was strengthened by the better facilities of the larger town, and the establishment of a rival school was forestalled. In June, 1879, the faculty adopted the articles of confederation and the standards of the Association of American Medical Colleges, and under date of August 30, 1880, it is noted in the faculty minutes that the school had been admitted to membership in this association.

Dr. E. P. Fraser was elected dean in 1880, and in October, 1884, plans for a medical school building were discussed. The need of such a building had been recognized for some time. In May, 1884, the Board of Trustees of the university had authorized its financial agent to devote part of his time to securing funds for the proposed building. In 1886, construction was begun and the building, which was a source of pride to the school, was occupied in 1887. It contained a dissecting room with a capacity of twenty tables, a refrigerating plant large enough to care for thirty bodies, and an auditorium with a seating capacity of one hundred fifty people. For its time it appears to have been well designed and equipped.

Educational requirements were not rigid, but this was generally true of American medical schools. In 1877, the requirements for admission provided that applicants must satisfy the dean of the medical faculty that he possessed the elements of a good English education. Previous to this time the requirements had been ill defined, and the adoption of the above regulation resulted in a diminished attendance. The course of lectures still continued 20 weeks and attendance at two courses was required. In 1883, this was increased to attendance on three courses of lectures, with certain specifications as to sequence of subjects. An attempt was made in 1884 to institute a preliminary course of 1 month, before medical instruction was begun.

In 1887, as the school was about ready to occupy the new building, a serious schism developed in the faculty. The causes are somewhat obscure, but appeared to involve some changes in the staff. As a result, the entire faculty resigned. Dr. E. P. Fraser, the dean, however, continued as acting dean. A new faculty was appointed by the Willamette Board, which included many of the men who had resigned and some new names from among practitioners of Portland. Several of the more outstanding members of the old faculty, however, were not included. These, together with other prominent physicians of the city, organized a second medical school, which through connections with the president of the Board of Regents of the State University, was taken under the ægis of the latter school and called the University of Oregon Medical School. Rivalry was bound to result, and for a time there was much bitterness. The faculty of the new school controlled the better hospital facilities, and the Willamette Medical Department, in spite of its new building, found itself in difficulties. It continued to give instruction in Portland until 1895, when the Methodist Hospital, its last hospital connection, was closed. The school found itself entirely without hospital facilities. The faculty appealed to the Board of Trustees of Willamette University for aid. Apparently nothing could be done in Portland, and the Board was unwilling to see the school die after 28 years of continuous history, so they provided quarters for it again at Salem.

The citizens of Salem subscribed funds for a new brick building on the Willamette campus, which was erected for the medical department,

and into which it moved in 1905. The department continued to occupy this building until 1913, when it was discontinued by merger with the University of Oregon Medical School, which in the meantime had outgrown the older school. The number of students in 1908–1909 was thirty-four, but increased to sixty in 1911–1912. When the school discontinued in 1913, there were two hundred thirteen alumni on its roll since the first class of 1867. This alumni roll is an honorable one. It includes many of the best known and best loved physicians of Oregon and the Northwest.

After its return to Salem in 1895, the school made a valiant struggle for existence, but with the handicaps of very limited funds and scarcity of material in this smaller city, it was impossible to maintain the standards set by the Council on Medical Education. The famous Flexner report of 1910 on "Medical Education in the United States" scored the Willamette Medical Department very severely, but in spite of this it continued to attract increasing numbers of students. Dr. W. H. Byrd, the dean during its last years at Salem, made every effort to build it up, but the task was too great to accomplish with very limited financial resources. After brief negotiations the merger with the stronger medical school of the State University, to which reference has already been made, was accomplished on March 23, 1913, under an agreement which protected the alumni of the older school.

In the light of present standards of medical education, the Willamette Medical Department, in common with very many of its contemporaries, had serious shortcomings. During all of its history it suffered from handicaps of poor equipment, dissensions in its faculty, and difficulties of all sorts, in a thinly populated state, far removed from centers of medical education. It struggled on as long as was possible and gave of the best it had to the young men and women who were eager for medical training, but who did not find it possible, early in their course at least, to go to the larger medical centers of the East.

Building erected in 1905 for Willamette Medical School at Salem, Oregon, after the school moved back to Salem.

To the memory of the school founded under pioneer conditions, we may now lay a wreath in honor of its having accomplished the expectation of the Board of Trustees of Willamette University who first launched the school in 1865, in the belief "that the interests of the country would be promoted."

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THE SURGEON'S LIBRARY

REVIEWS OF NEW BOOKS

ALMOST complete and comprehensive study of the world literature on uterosalpingography and induced pneumoperitoneum, together with the author's own experiences and technique for both procedures, is to be found in Jarcho's contribution to the *Annals of Roentgenology*.[1] The various techniques are well described and the book is profusely and adequately illustrated. From the number and quality of the roentgenograms reproduced, one must conclude, first, that the author has had a large experience with these procedures and, second, that he has developed an almost perfect technique for the reproduction of pelvic pathology on the roentgen film. The description of the author's technique, however, is difficult to follow and his statements of his method of roentgen reproduction are too indefinite unless one is familiar with his exact procedure.

In the chapters on combined pneumoperitoneum and uterosalpingography, the author states: "I myself now almost invariably give my patients preliminary insufflations of oxygen or carbon dioxide before taking uterosalpingograms," and yet the reviewer is struck by the paucity of films illustrating this combination method. Many of the films reproduced in this atlas could have made the diagnosis of existing pathology easier if the combination method had been employed. To one who has been privileged to see the advantages of the combination method as developed by Stein and Arens, this would seem to be a weakness. That the author himself favors the combination method is emphasized by a further statement (page 180). "The following cases illustrate clearly the superior visualization obtained by the combination method and its outstanding advantages in the diagnosis of obscure diseases of the pelvic and abdominal cavities."

An excellent chapter on radiation therapy includes a discussion of the various methods of X-ray and radium therapy, their indications and contraindications. The technique of radium therapy together with dosages and filtrations is also fully explained.

The bibliography of over 1100 references and the authors' index are most valuable for the worker in this field and help to make this volume a most desirable and necessary addition to the modern gynecological and roentgenological library. From the point of view of a gynecologist, a division of chapters according to the various types of pelvic pathology would have made this atlas even more desirable than it is at present. It should prove to be a valuable addition because of its completeness, its bibliography and authors' index, and mostly because of the excellent quality of the roentgenogram reproductions.

RALPH A. REIS

THE nomenclature of brain tumors is in a chaotic condition. Different names indicating different conceptions of histogenesis are applied to one and the same tumor by different pathologists. The purpose of the *Atlas du Cancer*[2] is to accomplish a unification not by words, but by pictures. "In the future it should be sufficient to give the page and number of a picture in this atlas in order to indicate the microscopic appearance of the brain tumor which one wants to describe." The authors believe that the histology of brain tumors indicates their relationship to certain embryonic forms. But the attempt to correlate a given tumor cell to ancestors of glia cells or neurons leads them away from their original goal to give merely a detailed histological description. They create the group of the "neurospongiomata," composed of apolar and unipolar neuroblasts, the same tumors which Bailey and Cushing classify as a more primitive medulloblastoma, and which, much to the surprise of the reader, they compare to the spongioblastoma of Globus and Strauss. Different spongioblastomata are grouped together as glioblastomata, and other groups like the astroblastomata of the American school are described as astrocytomata. They differentiate further between ependymoblastomata and ependymomata, after Bailey and Cushing had abandoned this subdivision.

The colored reproductions are excellent. They make it possible to identify most of the more common brain and peripheral nerve tumors, and will help the neurologic surgeon to classify his tumor material on a descriptive basis, without being involved in the controversies of the neuropathologists as to the embryonic origin.

ARTHUR WEIL

THE principal advantage of this excellent work[3] by Hoffmann lies in the series of roentgenograms in the same case to show the course and the prognosis of the most important bone and joint diseases, constituting a distinct improvement over an atlas of

[1] ANNALS OF ROENTGENOLOGY: A SERIES OF MONOGRAPHIC ATLASES. Edited by James T. Case, M.D. Vol. xiii—GYNECOLOGICAL ROENTGENOLOGY. By Julius Jarcho, M.D., F.A.C.S. New York: Paul B. Hoeber, Inc., 1931.

[2] ATLAS DU CANCER. Vols. ix and x—LES TUMEURS DES CENTRES NERVEUX ET DES NERFS PÉRIPHÉRIQUES. By Gustave Roussy and Charles Oberling. Paris: Librairie Felix Alcan, 1931.

[3] VERLAUF DER WICHTIGSTEN KNOCHEN UND GELENKERKRANKUNGEN IM ROENTGENBILDE: EINE AUSCHAULICHE PROGNOSTIK. By Privatdozent Dr. med. Victor Hoffmann. Berlin: Julius Springer, 1931.

miscellaneous illustrations. In other words, the work shows the various stages of a disease in one and the same case and not the different stages of a disease in different patients. The various cases chosen very satisfactorily cover the whole subject of bone and joint diseases. Sufficient clinical data accompanies each roentgenogram. A valuable contribution which will prove useful to radiologists, orthopedists and general surgeons. JAMES T. CASE

THE radiophysiology and the physical bases are the same whether radiotherapy be deep or superficial. The term deep therapy has come to be used in designating the technique, and especially the delivery, of a sufficient depth dose of high voltage X-radiation filtered through heavy metals. Employing a minimum of algebraic formulæ, the authors of *Radiotherapie*[1] present the physical data necessary for radiotherapy. Much space is devoted to radiophysiology. The third section sets forth a rational method of irradiation based on the physical and radiophysiological data. The final section is a clinical application of the foregoing. The work is well written, fairly complete, readable, and very helpful.
JAMES T. CASE

ALTHOUGH written by ten authors *Midwifery*[1] has overcome some of the disadvantages of collective authorship because the whole corps acted in an editorial and revisional capacity on every chapter of the book. All ten authors are teachers in London medical schools and among them are represented eight general hospitals with medical schools and three large lying-in hospitals.

In the treatment of eclampsia, conservatism is favored. However, general anæsthesia is looked upon as more advantageous than spinal or local anæsthesia for the delivery of women with toxæmia. This idea is contrary to the belief of most American obstetricians who are convinced that all inhalation anæsthetics, especially chloroform, have some deleterious effect on the important abdominal viscera particularly the liver. Furthermore a general anæsthetic increases the risk of pneumonia, and eclamptic patients are especially susceptible to this complication. The authors also suggest the use of veratrum viride and mild diuretics both of which are rarely employed by American obstetricians.

In the treatment of infected incomplete abortion, active intervention is recommended and the finger is considered less harmful than a sharp curette. In this country as well as on the continent most individuals favor conservative therapy for cases of septic abortion.

The treatment of advanced extra-uterine pregnancy is outlined but the therapy of the far more frequent early cases of ectopic gestation is not mentioned. This is to be found in the companion volume on diseases of women.

The statement is made that "a syphilitic child born alive at full time rarely shows any evidence of syphilis until some weeks after birth." While this may be true of external manifestations, it is usually possible to find evidences of syphilis in the newborn by means of Roentgen-ray pictures of the long bones.

The sections devoted to syphilis, gonorrhœa, tuberculosis, and disturbances of the thyroid gland are briefly discussed in striking contrast to an entire chapter devoted to insanity and childbirth and to a chapter on artificial feeding of babies.

The authors say "Episiotomy, the practise of making two small lateral incisions one on each side of the middle line of the perineal body with the object of preventing a deep median tear, is a practise to be advised only in exceptional cases." This explanation and the illustration of an episiotomy indicate that the authors are not familiar with episiotomies as practised rather extensively in the United States.

Regarding pituitary extract, the statement is made that it cannot be used to induce labor and that it is most useful in the later part of the second stage. However, many obstetricians have not infrequently been able to induce labor by means of this substance and unlike the authors have found that when it is given late in the second stage, especially in ½ cubic centimeter doses as recommended, it may result in disaster for the child or the mother.

The type of cæsarean section described and illustrated is the classic one. The low, cervical transperitoneal operation which is finding more and more favor throughout the world is not even mentioned in this book.

In spite of these criticisms the book will prove to be very helpful to students and general practitioners. It is written in a very readable style, the illustrations are abundant and instructive and the typography is clear. J. P. GREENHILL

[1] RADIOTHERAPIE: TECHNIQUE DU DOSAGE EN PROFONDEUR. By Charles Guilbert. Paris: N. Maloine, 1932.

[1] MIDWIFERY. By Ten Teachers. Edited by Comyns Berkeley, M.A., M.D., M.C. (Cautab), F.R.C.P. (Lond.), F.R.C.S. (Eng), F.C.O.G., J. S. Fairbairn and Clifford White. 4th ed. New York: William Wood and Co., 1931.

CORRESPONDENCE

To the Editor.

In SURGERY, GYNECOLOGY AND OBSTETRICS of September, 1931, there appeared a letter over the signature of W. Blair Bell in which there is an intimation of carelessness on my part in the review of the literature or an unwillingness to admit priority when compiling the bibliography of the article, "An Histologic Study of the Perivaginal Fascia in a Nullipara," which was published in SURGERY, GYNECOLOGY AND OBSTETRICS of January, 1931. I shall be obliged to you if you will publish my reply to the letter of Dr. Bell.

In the first edition (1910) of *Principles of Gynecology* by W. Blair Bell, there is a photomicrograph of the vesicovaginal septum and a similar one of the rectovaginal septum. No statement is made concerning either the parity of the woman from whom the sections were taken or the levels in the septa from which they were cut. When my article was submitted for publication I was unaware of the existence of these photomicrographs. My failure to find them when searching through the literature was due to the following reasons: (1) They were published in an elementary textbook, which, in the words of the author, was "undertaken with the object of presenting to the general practitioner and student (undergraduate, no doubt) a complete and modern survey of the foundations on which gynecology is established." It was quite natural to overlook a book of this sort when searching through the monographs on pelvic anatomy and vaginal plastic surgery. (2) Unfortunately these photomicrographs, which are very important, have not been quoted in the outstanding articles on pelvic anatomy or vaginal plastic surgery.

Dr. Bell makes the following statement in his letter: "Photomicrographs are shown of sections through the anterior vaginal wall and bladder, and the posterior vaginal wall and rectum, and the various structures are indicated." No fascia is mentioned, only "vaginal muscle." It is impossible to reconcile this statement with these excerpts from the text accompanying the photomicrographs:

1. "The relations of the vagina are important, for it is only separated from the bladder and urethra in front, and from the rectum behind, by connective tissue, which contains bundles of muscle fibers and strands of fascia from the aponeurosis covering the levator ani muscles."

2. "Structure of the vagina. As already indicated, the vagina is surrounded by an investment of muscular and fascial offshoots containing blood vessels, lymphatics, and nerves."

3. "Technique of anterior colporrhaphy. Care must be taken that the separation is effected in the plane between the bladder wall and the muscular and fascial layer underlying the vaginal mucosa, not only in order that the separation may be easy, but also that the muscle and fascia may be sutured together subsequently."

4. "Final stages in the performance of anterior colporrhaphy (author's method). The mucosa and muscular and fascial layers, after the excision of the redundant flaps, are being sutured in the midline by means of a mattress and overlapping stitch."

I regret my failure to find Dr. Bell's contribution. In the future I shall be glad to include it in the bibliography of all articles I may write on pelvic anatomy or vaginal plastic surgery.

BYRON H. GOFF

CLINICAL CONGRESS OF AMERICAN COLLEGE OF SURGEONS

ALLEN B. KANAVEL, Chicago, *President* J. BENTLEY SQUIER, New York, *President-Elect*
FRANKLIN H. MARTIN, Chicago, *Director-General*
EVARTS A. GRAHAM, St. Louis, *Chairman, Committee on Arrangements*

PLANNING FOR THE 1932 CLINICAL CONGRESS IN ST. LOUIS

THE surgeons of St. Louis will be hosts to the Fellows of the American College of Surgeons and their guests at the twenty-second annual Clinical Congress to be held in that city October 17–21. An attractive program of clinics and demonstrations for their entertainment is being developed by the Committee on Arrangements of which Dr. Evarts A. Graham is chairman and Dr. F. A. Jostes secretary. All departments of surgery will be represented therein—general surgery, obstetrics, gynecology, orthopedics, urology, surgery of the eye, ear, nose and throat.

Operative clinics and demonstrations in the hospitals are scheduled for Monday afternoon at 2 o'clock and for the mornings and afternoons of each of the four following days. A preliminary program of the clinics and demonstrations is being prepared for publication in an early issue of SURGERY, GYNECOLOGY AND OBSTETRICS.

Clinics and demonstrations will be given at the medical schools, Washington University and St. Louis University, and at the following hospitals: Alexian Brothers, Barnard Free Skin and Cancer, Barnes, Bethesda, Christian, DePaul, Evangelical Deaconess, Firmin des Loges, Frisco Employes', Jewish, Lutheran, McMillan, Missouri Baptist, Missouri Pacific, Mount St. Rose, St. Anthony's, St. John's, St. Louis Children's, St. Louis City No. 1 and 2, St. Louis County, St. Louis Maternity, St. Luke's, St. Mary's, St. Mary's Infirmary, Shriners', United States Marine, United States Veterans No. 92.

Two important features of the general program are a conference on cancer clinics and a symposium on cancer to be presented at headquarters on Thursday, and an all-day conference on traumatic surgery and industrial medicine on Friday. There will be daily exhibitions of surgical motion picture films, both sound and silent, in the ballroom of the Statler Hotel.

A sub-committee in charge of the program for the section on surgery of the eye, ear, nose and throat has been appointed consisting of the following: L. W. Dean, Chairman, John Green, Max Goldstein, Harvey Howard, William H. Luedde and William E. Sauer. The recommendations of this committee insure an attractive program of clinics and scientific sessions for all those who are interested in these specialties.

The Central Executive Committee of the Congress is preparing programs for a series of five evening meetings to be held in the grand ballroom of the Jefferson Hotel. On Monday evening, at the presidential meeting, the president-elect, Dr. J. Bentley Squier, of New York, will be inaugurated and deliver the annual address. On the same evening Sir William I. DeCourcy Wheeler, of Dublin, Ireland, will deliver the annual John B. Murphy oration in surgery. For Tuesday, Wednesday and Thursday evenings eminent surgeons of the United States and Canada with distinguished visitors from abroad have been invited to present papers dealing with surgical subjects of present-day importance. On Friday evening at the annual convocation of the College the 1932 class of candidates for Fellowship in the College will be received.

The Congress opens at 10 o'clock on Monday morning with the annual hospital conference in the ballroom of the Jefferson Hotel. An interesting program of papers, round table conferences and practical demonstrations dealing with problems related to hospital efficiency is being prepared for presentation at the conference which will continue on Tuesday and Wednesday. Subjects of interest to surgeons, hospital trustees, executives and personnel generally will be discussed.

General headquarters for the Clinical Congress will be established at the Jefferson Hotel, 12th and

Locust Streets, where the ballroom, Crystal and Ivory rooms and foyers adjacent thereto on the mezzanine and second floors have been reserved for the exclusive use of the Congress for scientific meetings, conferences, registration and ticket bureaus, bulletin boards, executive offices, scientific and technical exhibitions, etc. The grand ballroom of the Statler Hotel at Washington and 9th Streets will be utilized daily for film exhibitions and certain scientific sessions.

An application for reduced railway fares on account of the meeting in St. Louis is pending before the railroad traffic associations and it seems assured that a rate of one and one-half the regular first-class one-way fare on the certificate plan will be in effect from all points in the United States and Canada.

ADVANCE REGISTRATION

Attendance at the St. Louis session will be limited to a number that can be comfortably accommodated at the clinics—the limit of attendance being based upon the result of a survey of the amphitheaters, operating rooms and laboratories in the hospitals and medical schools to determine their capacity for accommodating visitors. It will be necessary, therefore, for those who wish to attend the Clinical Congress in St. Louis to register in advance.

Attendance at all clinics and demonstrations will be controlled by means of special clinic tickets, which plan provides an efficient means for the distribution of the visiting surgeons among the several clinics and insures against overcrowding, as the number of tickets issued for any clinic will be limited to the capacity of the room in which that clinic will be given.

A registration fee of $5.00 is required of each surgeon attending the annual Clinical Congress, such fees providing the funds with which to meet the expenses of the meeting. To each surgeon registering in advance a formal receipt for the registration fee is issued, which receipt is to be exchanged for a general admission card upon his registration at headquarters. This card, which is non-transferable, must be presented in order to secure clinic tickets and admission to the evening meetings.

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F. A. Jostes, Secretary

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Fig. 4.

Fig. 2.

Chorio-Epithelioma of the Uterus.— Arthur H. Curtis